Supplementary Table 1. Summary of histological type and number of cancer cell lines screened for *DICER1* mutations

Tissue	Histology	Total Number of cell lines screened	Number of microsatellite stable cell lines screened
adrenal gland	adrenal cortical carcinoma	2	2
autonomic ganglia	neuroblastoma	35	35
biliary tract	bile duct/gallbladder carcinoma	6	6
bone	osteosarcoma	9	8
bone	Ewings sarcoma/PNET	20	20
bone	chondrosarcoma	1	1
bone	other	1	0
breast	carcinoma	45	42
central nervous system	glioma	52	51
central nervous system	primitive neuroectodermal tumor/medulloblastoma	7	7
cervix	carcinoma	13	12
endometrium	carcinoma	10	4
eye	retinoblastoma	1	1
gastrointestinal tract	carcinoma	1	1
haemopoietic and lymphoid tissue	haemopoietic neoplasm	47	37
haemopoietic and lymphoid tissue	lymphoid neoplasm	80	64
kidney	carcinoma	20	16
kidney	Wilms tumor	1	1
kidney	rhabdoid tumor	1	1
large intestine	carcinoma	40	24
liver	carcinoma	10	9
lung	carcinoma	150	137
lung	carcinoma endocrine tumor	4	4
oesophagus	carcinoma	22	21
oesophagus	other	1	1
ovary	carcinoma	19	13
ovary	germ cell tumor	1	1
ovary	other	1	1
pancreas	carcinoma	17	16
placenta	choriocarcinoma	2	2

pleura	mesothelioma	6	5
prostate	carcinoma	4	1
prostate	hyperplasia	1	1
salivary gland	carcinoma	1	1
skin	malignant melanoma	45	43
skin	carcinoma	1	1
skin	adnexal tumor	1	1
small intestine	carcinoma	1	1
soft tissue	rhabdomyosarcoma	7	5
soft tissue	sarcoma – other	11	10
soft tissue	leiomyoblastoma	1	1
stomach	carcinoma	20	14
stomach	other	1	1
testis	germ cell tumor	4	4
thyroid	carcinoma	12	11
upper aerodigestive tract	carcinoma	22	21
upper aerodigestive tract	other	1	1
urinary tract	carcinoma	18	17
vulva	carcinoma	3	3
unspecified	carcinoma	2	2

Supplementary Table 2. Primers used to amplify *DICER1* coding exons.

Exon	Multiplex Group	Forward Primer Sequence (5'-3')	Reverse Primer Sequence (5'-3')	Size (bp)
2	B	CCCTGCATGATTGTGTAATGG	AGAAGTGGGAGGCCTGAAAG	343
3	C	TTTTGTAAATTTATTGGAGGACG	TCTGCCAGAAGAGATTAAATGAG	429
4	A	GAGGATAACCTTGGAACTGTGG	CCTAAATCAGACAACCAAGGC	388
5	C	AATCCTCACTTATGATACAATGGC	GCCAAACTCCCAATATTGATAAC	348
6	A	TAGTGGCATTTCCACCAAAC	ATTCTTACTCTTGCCCATTCC	388
7	A	CCCACTGCTAACATTCTGGC	GAGCCGCATTAAGCATATTTTC	395
8	A	AAATCCCAGTTAAACCCCAC	TGCAGCGCATCACATCAC	623
9	B	GACCAAGACCGTTTTGTTAGG	GAGACCCTATGGGCACTTTG	333
10	D	CCCAAGAGCATGTGTGTCAG	TTCCTATGGATACAAAGAATAACAAAG	439
11	C	TGTAGGTACAGAGGCAGACAGC	AACCGCAAAATGTCAACAATAC	323
12	C	CAAATTCAGTAGAGGGGAAGAG	CAACACAAGGCTCCTGCTC	375
13	B	GGGCAGTGGTTTCATAGGTG	TTAAGATCAGCAAGTGAATAGCTC	282
14	B	TCCAGGTCCTTCTAACATAGTTCTG	GGAACTGAGATTTGATGTAGCG	307
15	B	GTCATGCCTCGGGTATTTTC	ACAGAAATGATGCTTTCTAGTGG	475
16+17	C	CTAGAAAGCATCATTTCTGTTCTG	ACCGTGCCCGACCTAGTG	648
18	B	TGTAAAGGTGCCATTTAGCTTC	TTTGTGTGCAAAGCATCTCC	589
19	C	AGCCCAAGAGGCTGTAGTTG	CGAATCATGCATTTAACTTGG	319
20	A	AAATCCCATTTGGCCTTAGAG	TCTGACCTCAGATTCTCATCTCC	508
21a	A	AAATTCAAATTGCTGTTGCTCTC	TTTGTTAGCATTTCCATCAAGG	553
21b	C	CTTTTGCCAAGGAAATCAGC	CGTTCTCATCCTCTGAGATTATCC	557
22	A	CTTCTCAGTCATTCATAAGGAGTATG	GCAAAACTCAAAGTCAAAACATC	732
23a	A	TTGAAATTATCCATAACCCTTGC	GCTGGTTAAATAGCAGCCC	609
23b	B	GACTTTGTGGTGGGGTTCTG	TACAAGGCCAACACGATGAG	606
24	B	AATCTTCTTCGGATTTGGGG	TGCCGTCAGAACTCTGAAAC	434
25+26	C	TCCAAGAAAAGAAACTACATCTGTG	AAATCTGACAACAGCACACCAC	537
27	C	TGCACACTAAATGCTGATTGAC	CAACTTTAAGTCTTCCTTTCCG	328

Supplementary Table 3. *DICER1* non-pathogenic variants

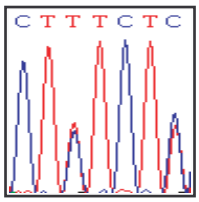
Nucleotide Change	Protein Change	Frequency
Non-synonymous variants		
c.20A>G	p.Q7R	3
c.1124C>G	pP375R	1
c.1381A>G	p.I461V	1
c.2254G>A	p.A752T	1
c.2614G>A	p.A872T	1
c.3392A>G	p.N1131S	1
c.4260_4262delGGA	p.D1421del	5
c.4802A>T	p.K1601M	1
c.4891T>G	p.S1631A	4
c.5740G>A	p.A1914T	1
Synonymous variants		
c.126T>C	p.Y42Y	1
c.366G>A	p.G122G	3
c.1191C>T	p.S397S	1
c.1887G>A	p.T629T	3
c.1935G>A	p.P645P	7 (rs61751177)
c.2115T>C	p.I705I	1
c.2370G>A	p.R790R	1
c.2658C>T	pD886D	1
c.2997T>G	p.L999L	7 (rs12018992)
c.3033G>A	p.A1011A	4 (rs8019857)
c.3198T>C	p.T1066T	3
c.3213A>G	p.R1071R	1
c.3813C>T	p.L1271L	1
c.3820A>C	p.R1274R	1
c.3972G>A	p.K1324K	3 (rs45562437)
c.4014G>A	p.A1338A	3
c.4647C>T	p.H1549H	1
c.4665T>C	p.A1555A	1
c.4680G>A	p.A1560A	4
c.4776G>T	p.P1592P	1
c.5112A>G	p.L1704L	1
c.5145C>T	p.L1715L	4
c.5643T>C	p.T1881T	1
Intronic variants		
c.439-7A>T		3
c.1377-4T>G		2
c.4207-3C>T		1
c.5769+4C>T		1
c.5769+5G>A		1

Supplementary Table 4. *DICER1* variants identified in cancer cell lines

Cell line	Tissue	Histology	Microsatellite Instability	DNA change	Protein change
ZR-75-30	breast	carcinoma	yes	c.946_962del	p.W316fs*15
NCI-H2342	lung	carcinoma	yes	c.3349G>T	p.E1117X
IGROV-1	ovary	carcinoma	yes	c.4605_4606delTG	p.C1535fs*3
MFE-296	endometrium	carcinoma	yes	c.5683C>T	p.R1895X
GR-ST	haematopoietic and lymphoid	haematopoietic neoplasm	yes	c.653A>G	p.E218G
TK10	kidney	carcinoma	no	c.835A>T	p.N279Y
HCT-116	large intestine	carcinoma	yes	c.862G>A	p.V288I
LS-411N	large intestine	carcinoma	yes	c.920G>A	p.R307H
HT-3	cervix	carcinoma	no	c.1213A>C	p.N405H
HCC2998	colorectal	carcinoma	no	c.1402G>A	p.D468N
HCT-15	large intestine	carcinoma	yes	c.1483G>A	p.E495K
CP66-MEL	skin	malignant melanoma	no	c.1504G>A	p.E502K
Ca9-22	upper aerodigestive tract	carcinoma	no	c.2033C>T	p.S678F
LAN-6	autonomic ganglia	neuroblastoma	no	c.2237G>C	p.R746T
NCI-H1770	lung	carcinoma	no	c.2612A>G	p.D871G
KYSE-520	oesophagus	carcinoma	no	c.3334A>G	p.N1112D
NCI-H1975	lung	carcinoma	no	c.3379A>T	p.I1127F
NCI-H1838	lung	carcinoma	no	c.3631G>T	p.V1211L
HEC-1	endometrium	carcinoma	yes	c.3673T>C	p.Y1225H
HCT-15	large intestine	carcinoma	yes	c.3839G>A	p.S1280N
SK-MES-1	lung	carcinoma	no	c.4123G>A	p.D1375N
PF-382	haematopoietic and lymphoid	lymphoid malignancy	no	c.4339C>A	p.Q1447K
ES4	bone	Ewings sarcoma	no	c.4474A>G	p.M1492V
HCC2998	large intestine	carcinoma	no	c.5001A>C	p.E1667D
NCI-H1522	lung	carcinoma	yes	c.5108G>A	p.R1703H
UACC-257	skin	malignant melanoma	no	c.5620T>C	p.Y1874H

Supplementary Figure 1. Constitutional *DICER1* mutations in 19 families

Family 1



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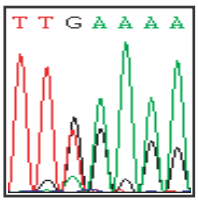
Family2



c.1716delT

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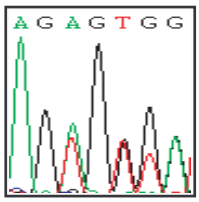

c.1196_1197dupAG

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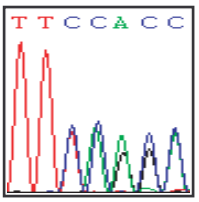

c.3505delT

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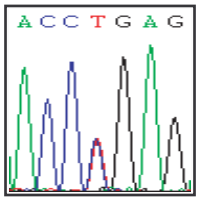

c.1996C>T

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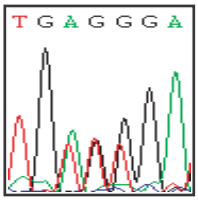
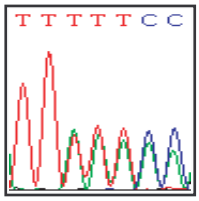


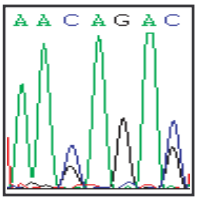
c.2268_2271delTTTG

Family 7



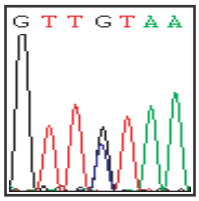
c.3665delT

Family 8



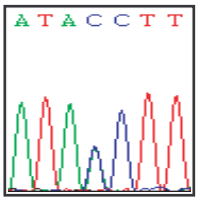
c.3583_3584delGA

Family 9



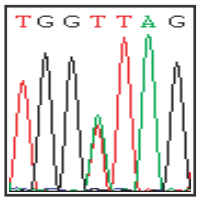
c.2040+1G>C

Family 10



c.3726C>A

Family 11



c.5465A>T

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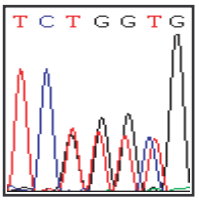
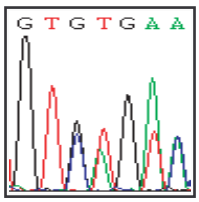


c.3288_3289insTTTC

Family13



c.328_338dup
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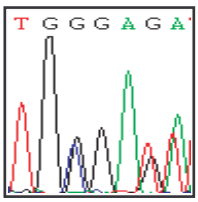
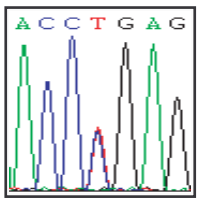
Family 14



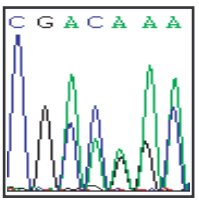
c.5122_5128
delGGAGATG

Family 15



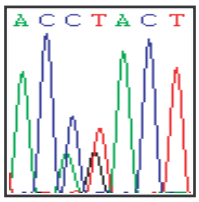
c.1966C>T

Family 16



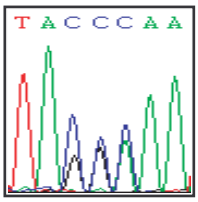
c.3793delA

Family 17



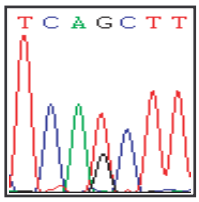
c.2988-2_2988-1
delAGinsCT

Family 18



c.1153delC

Family 19



c.4740G>T

APPENDIX

The FACT case series were recruited from the Paediatric Oncology Departments at the following centres. The lead co-ordinators for each centre are listed but we gratefully acknowledge all the clinical professionals involved in case recruitment at each centre: Aberdeen (M. Connon), Birmingham (J. Cooper and B. Morland), Bristol (S. Peters, R. Elson and M. Stevens), Cambridge (J. Tunnacliffe and A. Burke), Cardiff (J. Powell and H. Traunecker), Dublin (C. Rooney, A. O'Meara, M. Capra and J. Pears), Glasgow (W. Taylor and E Simpson), Great Ormond Street Hospital (K. Howe and G. Levitt), Leeds (U. Reid and A. Glaser), Liverpool (S. Hemsworth and H. McDowell), Manchester (L. Auld, C. Beane, B. Brennan and J. Birch), The Royal Marsden Hospital (R. Browning and K. Pritchard-Jones), Newcastle (L. Price and J. Hale), Nottingham (J. Evans, L. Whiles and D. Walker), Oxford (J. Coaker, K. Ashton and C. Mitchell), Southampton (J. Grout and M. Radford), Sheffield (M. Gerrard).