Supplementary Table S5

Gene	Mutation	In structure?	Surface/buried	Implication/comment	Predicted impact on structural integrity	MutatorAssessor Func. Impact	MutatorAssessor FI score	Polyphen-2 Prediction	Polyphen-2 score
ANAPC1	E139Q	No				low	1.5	benign	0.308
ANAPC1	F211V	Yes	Buried	Destabilising	Mild/Strong	medium	2.83	probably damaging	0.992
ANAPC1	G602D	Yes	Surface	Allows bend at loop; G>D destabilising	Strong	medium	2.02	probably damaging	0.973
ANAPC1	H1661Y	Yes	Surface	Destabilising; H situates in hydrophilic environment	Mild/Strong	medium	2.155	possibly damaging	0.826
ANAPC1	H27R	Yes	Buried	Destabilising	Strong	low	0.895	probably damaging	0.981
ANAPC1	M525V	No				low	1.32	benign	0.001
ANAPC1	N280K	Yes	Buried	Destabilising	Strong	medium	2.015	benign	0.18
ANAPC1	P314S	No				medium	2.32	probably damaging	0.993
ANAPC1	P558L	No				low	1.575	benign	0.001
ANAPC1	Q846P	Yes	Buried	Destabilising	Strong	medium	1.95	benign	0.261
ANAPC1	R1726T	No				low	1.69	benign	0.442
ANAPC1	R453L	Yes	Partially buried	Destabilising	Strong	medium	2.36	probably damaging	0.993
ANAPC1	R871K	Yes	Surface	Solvent exposed	None	neutral	-0.88	benign	0
ANAPC1	Y1552C	Yes	Buried	Destabilising	Strong	medium	3.41	probably damaging	0.999
ANAPC1	L1770F	Yes	Buried	Part of interface with Apc5; end of helical repeat	Mild. Similar side chain property.	neutral	-0.08	benign	0.003
ANAPC1	L230I	No	Surface	On a loop of Apc1 WD40 domain	N/A	neutral	0.69	benign	0
ANAPC1	D568N	No	Surface	Surface extended loop; not in sturcture	N/A	neutral	0.585	possibly damaging	0.455
ANAPC1	P1658S	Yes	Buried	Surface on beta jelly roll domain. Interface between PC repeat and beta jelly roll domain.	Mild	medium	2.645	benign	0.295
ANAPC1	P517T	No	Surface	On a loop of Apc1 WD40 domain.	None	low	1.2	benign	0.001
ANAPC1	D52N	Yes	Buried	On a loop between domains of Cdc23	Mild	low	1.15	probably damaging	0.997
ANAPC1	F1592L	Yes	Buried	At the central helices of PC repeat	Mild. Similar side chain property.	low	1.24	probably damaging	0.99
ANAPC1	E219K	Yes	Buried	Interacts with R458 of Cdc23	Mild	medium	2.64	probably damaging	0.995
ANAPC1	R1600W	Yes	Surface	On a surface loop forming interface with Apc10; may disrupt Apc10 binding	Stong	medium	2.525	probably damaging	0.995
ANAPC1	T416M	No	Surface	On a loop of Apc1 WD40 domain.	None	low	1.59	benign	0.431
ANAPC1	E772K	Yes	Buried	At the end of a helix; interacts with main chain to stabilise turn; destabilising	Strong	medium	2.36	benign	0.083
ANAPC1	S615C	Yes	Buried	On a surface loop forming interface with Apc5	Mild	medium	2.445	probably damaging	0.999
ANAPC1	S341L	No	N/A	Sites of CDK-dependent phosphorylation of Apc1, likely to contribute to APC/C activation in mitosis (Zhang et al., 2016)	N/A	low	1.7	probably damaging	0.981
ANAPC1	S736L	No	N/A	N/A	N/A	neutral	0.55	benign	0
ANAPC1	L1651F	Yes	Buried	May disrupt the structure of the jelly roll domain	Mild. Similar side chain property.	medium	2.015	benign	0.435
ANAPC1	S355F	No	N/A	Sites of CDK-dependent phosphorylation of Apc1, likely to contribute to APC/C activation in mitosis (Zhang et al., 2016; Kraft et al EMBO 2003)	N/A	low	1.935	probably damaging	0.99
ANAPC1	V471A	Yes	Surface	On the surface of of Apc1 WD40 beta propeller blade	None	low	1.18	possibly damaging	0.765
ANAPC1	Q1665L	Yes	Buried	Outside surface of central beta sheet.	None	low	1.5	benign	0.039
ANAPC1	L1928V	Yes	Surface	Side chain chemistry preserved	Mild	low	1.04	possibly damaging	0.956
ANAPC1	S1530L	Yes	Buried	Surface on PC repeat. Interface between PC repeat and beta jelly roll domain.	Mild	medium	2.575	possibly damaging	0.816
ANAPC1	L1662I	Yes	Buried	Surface on beta jelly roll domain. Interface between PC repeat and beta jelly roll domain.	Mild	low	1.405	possibly damaging	0.455
ANAPC2	D395H	Yes	Buried	Destabilising	Strong	medium	3.305	probably damaging	1
ANAPC2	E610D	Yes	Partially buried	Salt bridged preserved	Mild	low	1.55	benign	0.008
ANAPC2	F515I	Yes	Buried	Mildly destabilising; Hydrophobicility and size preserved	Mild/Strong	medium	2.65	probably damaging	1
ANAPC2	G193E	No				low	0.895	benign	0.001
ANAPC2	K495N	Yes	Partially buried	Salt bridge disrupted	Mild/Strong	low	1.525	probably damaging	0.601
ANAPC2	L514F	Yes	Buried	Mildly destabilising; Hydrophobicility and size preserved	Mild	medium	2.415	probably damaging	0.999
ANAPC2	R408S	Yes	Partially buried	Salt bridge disrupted	Mild/Strong	medium	2.43	probably damaging	0.992
ANAPC2	P482L	Yes	Surface	Loop forms interface with Apc1.	Mild	medium	3.3	probably damaging	1

Supplementary Table S5 (continued)

Gene	Mutation	In structure?	Surface/buried	Implication/comment	Predicted impact on structural integrity	MutatorAssessor Func. Impact	MutatorAssessor FI score	Polyphen-2 Prediction	Polyphen-2 score
ANAPC2	Y622H	Yes	Buried	Destabilises sheet-helix interaction between Apc2 and Apc11; may compromise ubiquitination eficiency	Strong	medium	3.15	probably damaging	1
ANAPC2	R340H	Yes	Buried	Destablises hairpin between helical pair on Apc2; may compromise substrate ubiquitination eficiency	Strong	medium	2.005	probably damaging	0.982
CDC27 (APC3)	E511K	Yes	Buried	Salt bridge disrupted. Predicted to disrupt the IR-tail binding site of co-activators and APC10	Strong	medium	2.585	probably damaging	1
CDC27 (APC3)	L474V	Yes	Partially buried	Hydrophobicity preserved	Mild	low	1.2	benign	0.002
CDC27 (APC3)	R130W	Yes	Buried	Salt bridge disrupted	Strong	medium	2.14	probably damaging	1
CDC27 (APC3)	S379L	No				medium	1.995	probably damaging	0.996
CDC27 (APC3)	S553L	Yes	Buried	Bulky mutation	Strong	medium	3.265	probably damaging	1
CDC27 (APC3)	S566L	Yes	Partially buried	On loop; mild	Mild	medium	3.04	probably damaging	0.996
CDC27 (APC3)	S761F	Yes	Buried	Destabilising	Strong	medium	3.02	probably damaging	1
CDC27 (APC3)	Y496C	Yes	Buried	Hydrophobicity and size preserved	Mild	medium	2.085	probably damaging	1
CDC27 (APC3)	R266Q	No	N/A	N/A	N/A	low	1.04	possibly damaging	0.921
CDC27 (APC3)	G248E	No	N/A	N/A	N/A	neutral	0	benign	0.097
CDC27 (APC3)	P246S	No	N/A	N/A	N/A	neutral	0.345	benign	0
CDC27 (APC3)	R629K	Yes	Surface	At an interface with Apc7 / Cdc16	Mild	low	1.84	possibly damaging	0.851
CDC27 (APC3)	D597H	Yes	Surface	Solvent exposed	Mild	medium	3.41	probably damaging	0.995
CDC27 (APC3)	G506E	Yes	Buried	Mutation could disrupt hydrophobic core. Predicted to disrupt the IR-tail binding site of co-activators and APC10	Strong	medium	2.765	probably damaging	1
CDC27 (APC3)	L144V	Yes	Surface	On a loop between two helices	Mild. Similar side chain property.	low	1.905	possibly damaging	0.747
CDC27 (APC3)	A273T	No	N/A	N/A	N/A	low	0.895	benign	0.014
CDC27 (APC3)	V25F	Yes	Buried	On a loop between two helices	Mild. Similar side chain property.	low	1.83	probably damaging	0.996
CDC27 (APC3)	A274D	No	N/A	N/A	N/A	neutral	0.695	benign	0.363
CDC27 (APC3)	S252T	No	N/A	N/A	N/A	neutral	0.695	benign	0
CDC27 (APC3)	S177I	No	N/A	N/A	N/A	neutral	0.695	benign	0.177
CDC27 (APC3)	S252F	No	N/A	N/A	N/A	neutral	0.695	benign	0.162
CDC27 (APC3)	N213D	No	N/A	N/A	N/A	neutral	0.695	benign	0.167
CDC27 (APC3)	H490Q	Yes	Surface	Outside of TPR/HEAT repeat; solvent exposed	None	neutral	-1.65	benign	0
CDC27 (APC3)	I487V	Yes	Surface	Mildly destabilising; hydrophobicility preserved	Mild	low	0.935	benign	0.024
ANAPC4	D694G	Yes	Buried	Salt bridge disrupted	Mild/Strong	low	1.32	benign	0.024
ANAPC4	P378L	Yes	Buried	P allows loop bending; P>L disrupts loop	Strong	low	1.59	possibly damaging	0.811
ANAPC4	Q335H	Yes	Surface	Solvent exposed	None	low	1.15	probably damaging	0.999
ANAPC4	R739C	Yes	Surface	Charged to hydrophobic	Mild	low	1.495	probably damaging	1
ANAPC4	R250Q	Yes	Buried	At interface with Apc5	Mild	low	1.04	probably damaging	0.996
ANAPC4	H114R	Yes	Buried	In centre of WD40 barrel; a relatively small change	Mild	low	0.84	benign	0.146
ANAPC4	L167P	Yes	Buried	Intra-domain stabilisation	Mild	medium	2.175	probably damaging	1
ANAPC4	R739C	Yes	Surface	Solvent exposed	None	low	1.1	probably damaging	1
ANAPC4	R12W	Yes	Surface	Solvent exposed	None	low	1.355	probably damaging	0.974
ANAPC5	A734V	Yes	Buried	A and V are similar	Mild	medium	1.975	probably damaging	0.995
ANAPC5	D517G	Yes	Partially buried	Salt bridge disrupted	Mild/Strong	low	0.805	possibly damaging	0.89
ANAPC5	R434C	Yes	Partially buried	Salt bridge disrupted - Destabilizing	Strong	neutral	0.69	probably damaging	0.998
ANAPC5	S118F	Yes	Buried	Bulky mutation	Strong	medium	2.015	possibly damaging	0.855
ANAPC5	S208F	Yes	Buried	Bulky mutation	Strong	medium	2.255	possibly damaging	0.938
ANAPC5	S611F	Yes	Buried	Bulky mutation	Strong	low	1.5	possibly damaging	0.612
ANAPC5	E542Q	Yes	Surface	In the centre of TPR barrel; may disrupt interaction with Apc15.	Mild	low	1.5	probably damaging	1
ANAPC5	A734V	Yes	Buried	May interfere with Emi1 binding	Strong	low	1.795	probably damaging	0.995
ANAPC5	P498S	Yes	Buried	Forms loop between two helices of TPR repeats	Mild	low	1.795	probably damaging	1
ANAPC5	N91D	Yes	Surface	Solvent exposed	None	low	0.895	benign	0.094
ANAPC5	D226V	Yes	Buried	Interace between TPR stacks.	Mild	low	1.795	probably damaging	1
ANAPC5	A600T	Yes	Buried	Between helices.	Strong	low	1.895	probably damaging	0.999

Supplementary Table S5 (continued)

Gene	Mutation	In structure?	Surface/buried	Implication/comment	Predicted impact on structural integrity	MutatorAssessor Func. Impact	MutatorAssessor FI score	Polyphen-2 Prediction	Polyphen-2 score
ANAPC5	P233T	Yes	Surface	Forms loop between two helices.	Mild	medium	2.215	probably damaging	1
ANAPC7	A242V	Yes	Buried	A similar to V	Mild	low	1.665	probably damaging	0.998
ANAPC7	P302S	Yes	Buried	P on loop; P>S disrupts loop bending	Strong	low	1.04	probably damaging	1
ANAPC7	V450I	Yes	Partially buried	Hydrophobicity preserved	Mild	low	1.095	possibly damaging	0.547
ANAPC7	Y93C	Yes	Buried	Hydrophobicity and size preserved	Mild	low	0.975	probably damaging	0.996
ANAPC7	S86F	Yes	Buried	Packs between 2 helices>F would probably destabilise dimer interface.	Strong	low	1.2	probably damaging	0.996
ANAPC7	L207V	Yes	Surface	Inside of TPR/HEAT crescent.	Mild	low	0.895	benign	0.047
ANAPC7	E144K	Yes	Surface	Inside of solvent accessible channel between dimer.	None	neutral	0.345	benign	0.002
ANAPC7	E415K	Yes	Surface	Inside of TPR/HEAT crescent.	None	low	1.245	possibly damaging	0.618
ANAPC7	T190I	Yes	Surface	Solvent exposed.	None	low	1.24	possibly damaging	0.763
ANAPC7	D466N	Yes	Surface	Solvent exposed	None	low	0.895	probably damaging	0.974
ANAPC10	V74M	Yes	Buried	Destabilising; M is bulkier than V	Mild/Strong	medium	2.15	probably damaging	0.959
ANAPC10	H152D	Yes	Surface	At bipartite substrate recognition site; Close to D-box binding site, may disrupt substrate binding (Chang et al., 2015)	None	high	3.685	probably damaging	1
ANAPC11	P73S	Yes	Buried	Destabilising; P stacked between aromatic rings. Close to UbcH10-binding site, predict would impair UbcH10 binding	Strong	neutral	0.345	probably damaging	0.99
ANAPC11	A135T	No	N/A	N/A	N/A				
ANAPC11	E21Q	Yes	Surface	On a long surface loop	None	low	1.655	benign	0.436
ANAPC13	M55I	Yes	Surface	Forms interface with Cdc23.	Mild. Similar side chain property.	low	1.1	benign	0.001
CDC16	D27H	Yes	Buried	Salt bridge disrupted	Mild/Strong	medium	2.74	probably damaging	1
CDC16	D546G	No				low	0.895	possibly damaging	0.629
CDC16	D617H	No				low	0.975	probably damaging	0.999
CDC16	E603K	No				low	0.895	possibly damaging	0.455
CDC16	M610L	No				low	0.975	benign	0.167
CDC16	R55G	Yes	Buried	Salt bridge disrupted	Strong	medium	2.795	probably damaging	0.999
CDC16	N100K	No	Surface?	On a disordered loop in both subunits	N/A	neutral	0.55	benign	0.156
CDC16	L580R	No	N/A	N/A	N/A	neutral	0.345	benign	0.145
CDC16	L148M	Yes	Surface	Solvent exposed	None	low	1.055	possibly damaging	0.883
CDC16	H241N	Yes	Surface	Solvent exposed	None	low	1.04	benign	0.19
CDC20	P477A	No	Surface	On a loop connecting WD40 domain to IR motif; may disrupt coactivator binding.	Strong	neutral	0.69	probably damaging	1
CDC20	E111K	No		Glu111 forms a salt bridge with Lys114. Mutation would be predicted to be de-stabilizing. (Zhang et al., 2016)		medium	3.04	benign	0.376
CDC20	L151F	No		N-terminal; could disrupt APC interaction		medium	2.86	probably damaging	0.972
CDC20	P21S	No		N-terminal; could disrupt APC interaction		neutral	0.755	benign	0.001
CDC20	Q68R	No		N-terminal; could disrupt APC interaction		low	1.78	benign	0.005
CDC20	R132P	Yes (MCC structure)		Disrupt KILR motif; could disrupt APC/C and Mad2 binding	Disrupts MCC function	medium	2.005	possibly damaging	0.86
CDC20	R44L	No		N-terminal; could disrupt APC interaction		neutral	0.69	benign	0.149
CDC20	S268F	Yes (MCC structure)		Surface mutation on WD40 domain.	Mild	medium	2.69	benign	0.375
CDC23	I76F	Yes	Buried	Hydrophobicity and size preserved	Mild	neutral	-0.695	benign	0
CDC23	M84T	Yes	Buried	Destabilising	Mild/Strong	neutral	-0.695	benign	0.001
CDC23	P568R	No				low	1.24	benign	0
CDC23	R101L	Yes	Buried	Salt bridge disrupted	Strong	medium	3.36	possibly damaging	0.872
CDC23	S121F	Yes	Buried	Destabilising	Strong	medium	2.96	probably damaging	1
CDC23	T582P	No	N/A	N/A	N/A	low	1.5	benign	0.015
CDC23	V595A	No				neutral	0.69	benign	0.017

Supplementary Table S5 (continued)

Gene	Mutation
Truncating mutations:	
ANAPC1	W641*
ANAPC1	E1513*
ANAPC1	G1640_splice
ANAPC4	L79_splice
ANAPC4	S562_splice
ANAPC4	E186*
ANAPC4	R728*
ANAPC4	Q477_splice
ANAPC4	E293*
ANAPC4	A459_splice
ANAPC5	E49*
ANAPC5	E729*
ANAPC5	Q505_splice
ANAPC7	L464*
CDC16	E35_splice
CDC16	Q18*
CDC26	R23*
CDC27	E736*
CDC27	T320_splice
CDC27	Q793*
CDC20	E98*
CDC20	W470*