Supplemental Appendix

Supplement to: Koichi Takahashi and Boyu Hu, Feng Wang, Yuanqing Yan *et al.* Clinical Implications of Cancer Gene Mutations in Patients with Chronic Lymphocytic Leukemia Treated with Lenalidomide.

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Supplemental Method

Targeted gene sequencing of CLL samples and detection of high-confidence driver mutations

Genomic DNA was extracted from diagnostic BM aspirate or PB samples using an Autopure extractor (QIAGEN/Gentra, Valencia, CA). DNAs were fragmented and bait-captured in solution as previously described according to manufacturer protocols [1]. Captured DNA libraries were then sequenced using a HiSeq 2000 sequencer (Illumina, San Diego, CA) with 76 basepair (bp) paired-end reads. Raw sequencing data from the Illumina platform were converted to a fastq format and aligned to the reference genome (hg19) using the Burroughs-Wheeler Aligner (BWA) [2]. The aligned BAM files were subjected to mark duplication, re-alignment, and re-calibration using Picard and GATK (https://www.broadinstitute.org/gatk/guide/best-practices?bpm=DNAseq). Preprocessed BAM files were then analyzed to detect single nucleotide variants (SNV) and small insertions and deletions (indels) using MuTect [3] and Pindel [4] algorithms, respectively, against virtual normal sequence developed in-house.

We modified an approach described by Pappaemanuil et al. to identify high-confidence driver mutations in the bone marrow samples without matched germline control [5]. First, variants with low quality supporting sequencing data were filtered out. Specifically, variants matching one or more of the following criteria were considered of low quality and therefore filtered out from further analysis: 1) tumor coverage < 15x and 20x for single nucleotide variants (SNVs) and insertions/deletions (indels), respectively, 2) tumor allele frequency < 5%, and 3) normal allele frequency >= 1% and 0% for SNVs and INDELs, respectively. Second, only variants which would introduce an obvious protein-coding change were kept for further analysis. Specifically, variant with an ANNOVAR annotation of non-synonymous, stop-gain, stop-loss, splicing, frameshift insertion, frameshift deletion, non-frameshift insertion or non-frameshift deletion was considered to be able to introduce an obvious protein-coding change and were therefore kept for further analysis. Third, common polymorphisms were removed to reduce the load of possible germline contamination due to the absence of matched normal. Specifically, a series of public variant database including the 1000 Genome Database (http://www.1000genomes.org/), ESP6500 Database (http://evs.gs.washington.edu/EVS/), dbSNP ver.132 (https://www.ncbi.nlm.nih.gov/projects/SNP/snp_summary.cgi?build_id=132), and Exome Aggregation Consortium database (http://exac.broadinstitute.org/), were utilized. Variant with a population frequency of 0.14% or more in any of the databases was considered possible germline polymorphism and was therefore removed from further analysis. Finally, hierarchical classification system was developed to assign confidence level for each remaining variant in order to facilitate the identification of putative driver mutations. Specifically, each variant was classified based on the following hierarchical order and was assigned a confidence level corresponding to its rank in the system: 1) Confirmed somatic mutation based on COSMIC database (version 72), 2) loss-of-function mutation such as splicing, stop-gain, stop-loss and frameshift mutation in known tumor suppressor genes, 3) recurrent variant which resides within three amino acids away from a confirmed somatic mutation according to COSMIC database (version 72), 4) variant which resides within three amino acids away from a confirmed somatic mutation according to COSMIC database (version 72), 5) variant which was predicted to be damaging by in-silico function prediction algorithms, and 6) variant with unknown significance. The first three groups were considered high-confidence tier while the remaining were considered of low-confidence. The final annotated variant list was passed out of the pipeline and was further analyzed by manual inspection and literature mining in order to identify high-confidence driver mutations.

Table S1. Various lenalidomide based protocols performed at MD Anderson Cancer Center from 2005-2014 and their respective patient enrollments.

Protocol	Regimen	Treatment-naïve (n)	Relapsed/Refractory (n)
NCT00267059	**Lenalidomide**	**-**	**46**
NCT00535873	**Lenalidomide**	**46**	**-**
NCT00759603	**Lenalidomide plus Rituximab**	**-**	**55**
NCT01446133	**Lenalidomide plus Rituximab**	**56**	**53**
NCT01002755	**Lenalidomide plus Ofatumumab**	**-**	**32**

Table S2. List of 295 genes targeted by next generation sequencing.

Gene name									
ABCC9	*CALR*	*CUL5*	*FANCD2*	*HIST1H2BF*	*LEF1*	*NBN*	*PLA2G2D*	*SF3B1*	*TINF2 (TIN2)*
ABL1	*CARD11*	*CUX1*	*FANCE*	*HIST1H3D*	*LRP1B*	*NCOR1*	*PLCG2*	*SFRS1*	*TLR2*
ACTG1	*CBL*	*CYLD*	*FANCG*	*HIST1H4D*	*LTB*	*NCOR2*	*POT1*	*SFRS7*	*TLR9*
AKT1	*CBLB*	*DAXX*	*FANCI*	*HNRNPK*	*LUC7L2*	*NF1*	*POU2AF1*	*SGK1*	*TNFAIP3*
ANKRD11	*CCND1*	*DCLRE1C*	*FANCL*	*HRAS*	*LYN*	*NFE2*	*PRDM1*	*SH2B3*	*TNFRSF14*
ARID1A	*CCND3*	*DDX3X*	*FAS*	*ICOS*	*MALT1*	*NFKB1*	*PRKCB*	*SHH*	*TNKS*
ARID1B	*CD200*	*DIS3*	*FAT1*	*ID3*	*MAP2K1*	*NFKB2*	*PTEN*	*SMAD2*	*TOX*
ARID2	*CD274*	*DKC1*	*FAT3*	*IDH1*	*MAPK1*	*NFKBIA*	*PTPN1*	*SMC1A*	*TP53*
ARID5B	*CD58*	*DLC1*	*FBXW7*	*IDH2*	*MAX*	*NFKBIE*	*PTPN11*	*SMC3*	*TRAF3*
ARPP21	*CD79A*	*DNM2*	*FGFR3*	*IKBKA*	*MDM2*	*NOTCH1*	*RAD21*	*SMC5*	*TRAF6*
ASXL1	*CD79B*	*DNMT1*	*FLI1*	*IKZF1*	*MED12*	*NOTCH2*	*RAD51C*	*SNX7*	*TYK2*
ATF7IP	*CDK4*	*DNMT3A*	*FLT3*	*IKZF2*	*MEF2B*	*NPM1*	*RAG1*	*SOCS1*	*TYK3*
ATM	*CDKN2A*	*DNMT3B*	*FNDC3A*	*IKZF3*	*MEF2C*	*NR3C2*	*RAG2*	*SOX5*	*U2AF1*
ATRX	*CDKN2B*	*EBF1*	*FOXP1*	*IL7R*	*MGA*	*NRAS*	*RASA2*	*SP140*	*U2AF2*
B2M	*CDKN2C*	*ECT2L*	*FYN*	*IRAK1*	*miR125a*	*NSD2*	*RB1*	*SPEN*	*UBR5*
BCL10	*CEBPA*	*EED*	*G6PC3*	*IRAK4*	*miR-142*	*NT5C2*	*REL*	*SPIB*	*USP29*
BCL2	*CEBPE*	*EGR1*	*GAB2*	*IRF1*	*mIR155*	*PAG1*	*RELA*	*SRSF2*	*VPREB1*
BCL6	*CHD2*	*EGR2*	*GATA1*	*IRF4*	*mIR15a*	*PALB2*	*RELB*	*STAG1*	*WHSC1*
BCL7A	*CHK2*	*ELANE*	*GATA2*	*IRF7*	*mIR16-1*	*PAX5*	*RELN*	*STAG2*	*WHSC1L1*
BCOR	*CIITA*	*EP300*	*GATA3*	*ITPKB*	*MIR17HG*	*PDCD1*	*RHOA*	*STAT1*	*WT1*
BCR	*CNOT3*	*EPHA7*	*GCET2*	*JAK1*	*mIR21*	*PDCD1LG2*	*RIPK1*	*STAT3*	*XPO1*
BIRC3	*CREBBP*	*EPOR*	*GFI1B*	*JAK2*	*mir34b*	*PDGFRB*	*ROBO1*	*SUZ12*	*ZAP70*
BLK	*CRLF2*	*ERG*	*GNA13*	*JAK3*	*mir34c*	*PEG3*	*ROR1*	*SYK*	*ZMYM2*
BMI1	*CSF2RA*	*ETV6*	*GNAS*	*JARID2*	*MLL*	*PHF6*	*RPL10*	*TBL1XR1*	*ZMYM3*
BRAF	*CSF3R*	*EZH2*	*GNB1*	*KDM4C*	*MLL2*	*PHIP*	*RPL5*	*TCF3*	*ZRSR2*
BRIP1	*CTBP1*	*FAM46C*	*GPRC5A*	*KDM6A*	*MLL3*	*PIGA*	*RUNX1*	*TERC*	
BTG1	*CTBP2*	*FAM5C*	*HAX1*	*KIT*	*MPL*	*PIK3CA*	*RUNX2*	*TERT*	
BTK	*CTCF*	*FANCA*	*HIST1H1E*	*KLHL6*	*MS4A1*	*PIK3CB*	*SAMHD1*	*TET1*	
BTLA	*CTLA4*	*FANCB*	*HIST1H2AD*	*KRAS*	*MYB*	*PIK3CG*	*SETBP1*	*TET2*	
C22orf194	*CTNNA1*	*FANCC*	*HIST1H2BE*	*LAMB4*	*MYD88*	*PIK3R1*	*SETD2*	*TGDS*	

Table S3. List of all mutations detected.

Mutation Class	Gene	Transcript ID	Nucleotide change	AA change
exonic	*ARID1A*	uc001bmv.1	c.6746delC	p.S2249X
exonic	*ARID1A*	uc001bmv.1	c.6094_6095insAAAAGGAGGAGGAACAGGACCAAGGGGTGAGCTGCAACAAAGT	p.E2032fs
exonic	*ARID1A*	uc001bmt.1	c.2320_2327del	p.774_776del
exonic	*ASXL1*	uc021wbw.1	c.C2616A	p.C872X
exonic	*ASXL1*	uc021wbw.1	c.2523delA	p.V841fs
exonic	*ASXL1*	uc021wbw.1	c.2449_2450insT	p.L817fs
exonic	*ASXL1*	uc021wbw.1	c.2171delT	p.L724fs
exonic	*ASXL1*	uc021wbw.1	c.2556_2557insC	p.S852fs
exonic	*ASXL1*	uc021wbw.1	c.2849_2850insA	p.L950fs
exonic	*ASXL1*	uc021wbw.1	c.2569_2570insA	p.L857fs
exonic	*ATM*	uc001pkb.1	c.T7309G	p.Y2437D
exonic	*ATM*	uc001pkb.1	c.G8672A	p.G2891D
exonic	*ATM*	uc001pkb.1	c.G8151C	p.K2717N
exonic	*ATM*	uc001pkb.1	c.G9023A	p.R3008H
exonic	*ATM*	uc001pkb.1	c.C103T	p.R35X
exonic	*ATM*	uc001pkb.1	c.C8494T	p.R2832C
exonic	*ATM*	uc001pkb.1	c.G7267A	p.E2423K
exonic	*ATM*	uc001pkb.1	c.G7267A	p.E2423K
exonic	*ATM*	uc001pkb.1	c.A2314T	p.R772X
exonic	*ATM*	uc001pkb.1	c.C1120T	p.Q374X
exonic	*ATM*	uc001pkb.1	c.C7194A	p.Y2398X
splicing	*ATM*		Chr11:108143335,G>T	
splicing	*ATM*		Chr11:108188249,G>T	
exonic	*ATM*	uc001pkb.1	c.C8525T	p.P2842L
exonic	*ATM*	uc001pkb.1	c.A1G	p.M1V
exonic	*ATM*	uc001pkb.1	c.T9032A	p.M3011K
splicing	*ATM*		Chr11:108168110,G>C	
exonic	*ATM*	uc001pkb.1	c.G667T	p.E223X
exonic	*ATM*	uc001pkb.1	c.880delG	p.G294fs
exonic	*ATM*	uc001pkb.1	c.5599delC	p.Q1867fs
exonic	*ATM*	uc001pkb.1	c.1875_1876del	p.625_626del
exonic	*ATM*	uc001pkb.1	c.4096_4097del	p.1366_1366del
exonic	*ATM*	uc001pkb.1	c.361_362insTG	p.L121fs
exonic	*ATM*	uc001pkb.1	c.477_481del	p.159_161del
splicing	*ATM*		Chr11:108124536,TTGAAG>T	
exonic	*ATM*	uc001pkb.1	c.838_842del	p.280_281del
exonic	*ATM*	uc001pkb.1	c.4638_4641del	p.1546_1547del
exonic	*ATM*	uc001pkb.1	c.2282_2283del	p.761_761del
exonic	*ATM*	uc001pkb.1	c.580_581insT	p.V194fs
exonic	*ATM*	uc001pkb.1	c.7308delA	p.R2436fs
exonic	*BCL2*	uc002liu.1	c.C256T	p.L86F
exonic	*BCL2*	uc002liu.1	c.C157T	p.P53S
exonic	*BCOR*	uc004dem.4	c.2443_2444insT	p.A815fs
exonic	*BCOR*	uc004dem.4	c.3311delA	p.K1104fs

exonic	*BCOR*	uc004dem.4	c.3088_3089del	p.1030_1030del
exonic	*BCOR*	uc004den.4	c.4140_4141del	p.1380_1381del
exonic	*BCOR*	uc004den.4	c.4140_4141del	p.1380_1381del
exonic	*BCOR*	uc004dem.4	c.433_434del	p.145_145del
exonic	*BCOR*	uc004dem.4	c.3090_3093del	p.1030_1031del
exonic	*BCOR*	uc004dem.4	c.264_277del	p.88_93del
exonic	*BCOR*	uc004den.4	c.4097_4100del	p.1366_1367del
exonic	*BIRC3*	uc001pgx.3	c.T1754G	p.L585X
exonic	*BIRC3*	uc001pgx.3	c.T1337G	p.L446X
exonic	*BIRC3*	uc001pgx.3	c.1639delC	p.Q547fs
exonic	*BIRC3*	uc001pgx.3	c.1639delC	p.Q547fs
exonic	*BIRC3*	uc001pgx.3	c.1320_1321insT	p.E440fs
exonic	*BIRC3*	uc001pgx.3	c.1639delC	p.Q547fs
exonic	*BIRC3*	uc001pgx.3	c.1639delC	p.Q547fs
exonic	*BIRC3*	uc001pgx.3	c.1639delC	p.Q547fs
exonic	*BIRC3*	uc001pgx.3	c.1639delC	p.Q547fs
exonic	*BIRC3*	uc001pgx.3	c.1642delT	p.L548fs
exonic	*BIRC3*	uc001pgx.3	c.1276_1277insA	p.E426fs
exonic	*BIRC3*	uc001pgx.3	c.1641_1642insT	p.Q547fs
exonic	*BIRC3*	uc001pgx.3	c.1290_1291insGA	p.E430fs
exonic	*BIRC3*	uc001pgx.3	c.1318_1319insAATC	p.E440fs
exonic	*BIRC3*	uc001pgx.3	c.1281_1288del	p.427_430del
exonic	*BIRC3*	uc001pgx.3	c.1262_1263insCAATGCAGAAGATGAAATAAGGGAAG	p.L421fs
exonic	*BIRC3*	uc001pgx.3	c.1291_1292insA	p.E431fs
exonic	*BIRC3*	uc001pgx.3	c.1639delC	p.Q547fs
exonic	*BIRC3*	uc001pgx.3	c.1138delC	p.P380fs
exonic	*BRAF*	uc003vwc.4	c.T1790A	p.L597Q
exonic	*BRAF*	uc003vwc.4	c.A1803T	p.K601N
exonic	*BRAF*	uc003vwc.4	c.G1406C	p.G469A
exonic	*BRAF*	uc003vwc.4	c.A1803C	p.K601N
exonic	*BRAF*	uc003vwc.4	c.T1790A	p.L597Q
exonic	*BRAF*	uc003vwc.4	c.A1801G	p.K601E
exonic	*BRCC3*	uc004fna.3	c.G637T	p.E213X
exonic	*BRCC3*	uc004fna.3	c.C10T	p.Q4X
exonic	*BRCC3*	uc011mzy.2	c.C519A	p.C173X
exonic	*BRCC3*	uc011mzy.2	c.256delA	p.K86fs
exonic	*BRCC3*	uc011mzy.2	c.456delA	p.G152fs
splicing	*BRCC3*		ChrX:154305565,GAT>G	
exonic	*BRCC3*	uc004fna.3	c.782_783insGG	p.K261fs
exonic	*BRCC3*	uc011mzy.2	c.183_195del	p.61_65del
exonic	*BRCC3*	uc004fna.3	c.76_95del	p.26_32del
exonic	*CD79B*	uc002jdp.1	c.T624G	p.Y208X
exonic	*CHD2*	uc002bso.1	c.T2378A	p.L793X
exonic	*CHD2*	uc010urb.2	c.134_135insTG	p.D45fs
exonic	*CHD2*	uc002bso.1	c.4165_4168del	p.1389_1390del
splicing	*CHEK2*		Chr22:29121230,C>T	

exonic	*CHEK2*	uc003adt.1	c.C1140A	p.Y380X
exonic	*CHEK2*	uc003adt.1	c.720delA	p.K240fs
exonic	*CNOT3*	uc002qdk.2	c.G58A	p.E20K
exonic	*CNOT3*	uc002qdk.2	c.G58A	p.E20K
splicing	*CREBBP*		Chr16:3789726,C>T	
exonic	*CREBBP*	uc002cvv.3	c.C3436T	p.Q1146X
exonic	*CREBBP*	uc002cvv.3	c.2400delG	p.P800fs
exonic	*CREBBP*	uc002cvv.3	c.3469_3475del	p.1157_1159del
exonic	*DDX3X*	uc004dfe.3	c.C1582T	p.R528C
splicing	*DDX3X*		ChrX:41204656,G>C	
exonic	*DDX3X*	uc004dfe.3	c.A652T	p.R218X
exonic	*DDX3X*	uc004dfe.3	c.C43T	p.Q15X
exonic	*DDX3X*	uc004dfe.3	c.1470delA	p.G490fs
splicing	*DDX3X*		ChrX:41204428,TGACA>T	
splicing	*DIS3*		Chr13:73342922,C>A	
exonic	*DIS3*	uc001vix.4	c.C2065T	p.R689X
exonic	*DLC1*	uc003wwm.2	c.C1049T	p.A350V
exonic	*DNMT3A*	uc002rgc.3	c.T2578C	p.W860R
splicing	*DNMT3A*		Chr2:25468121,C>T	
exonic	*DNMT3A*	uc002rgc.3	c.G2384A	p.W795X
exonic	*DNMT3A*	uc002rgc.3	c.C2206T	p.R736C
exonic	*DNMT3A*	uc002rgc.3	c.G2645A	p.R882H
exonic	*DNMT3A*	uc002rgc.3	c.G2645A	p.R882H
splicing	*DNMT3A*		Chr2:25467408,C>T	
splicing	*DNMT3A*		Chr2:25467407,A>G	
exonic	*DNMT3A*	uc002rgc.3	c.C1988A	p.S663X
exonic	*EGR2*	uc010qio.2	c.C1189A	p.H397N
exonic	*EGR2*	uc010qio.2	c.G1105A	p.E369K
exonic	*EGR2*	uc010qio.2	c.C1189A	p.H397N
exonic	*EGR2*	uc010qio.2	c.G1105A	p.E369K
exonic	*EGR2*	uc010qio.2	c.G1270C	p.D424H
exonic	*EGR2*	uc010qio.2	c.G1270C	p.D424H
exonic	*EGR2*	uc010qio.2	c.G1105A	p.E369K
exonic	*EGR2*	uc010qio.2	c.A295T	p.R99X
exonic	*EGR2*	uc010qio.2	c.C1189A	p.H397N
exonic	*EGR2*	uc010qio.2	c.C1189A	p.H397N
exonic	*EGR2*	uc010qio.2	c.G1105A	p.E369K
exonic	*EGR2*	uc010qio.2	c.C1189A	p.H397N
exonic	*EGR2*	uc010qio.2	c.C1189A	p.H397N
exonic	*EGR2*	uc010qio.2	c.G1105A	p.E369K
exonic	*EGR2*	uc010qio.2	c.G1105A	p.E369K
exonic	*EP300*	uc003azl.4	c.A5711C	p.Q1904P
exonic	*EZH2*	uc003wfb.2	c.A965G	p.N322S
exonic	*FAT1*	uc003izf.3	c.G9358A	p.D3120N
exonic	*FAT1*	uc003izf.3	c.C6512T	p.P2171L
exonic	*FBXW7*	uc003ims.3	c.C1393T	p.R465C

exonic	*FBXW7*	uc003ims.3	c.A1136G	p.H379R
exonic	*FBXW7*	uc003ims.3	c.G1514T	p.R505L
exonic	*FBXW7*	uc003ims.3	c.G1310T	p.G437V
exonic	*FBXW7*	uc003ims.3	c.C1177T	p.R393X
exonic	*FBXW7*	uc003ims.3	c.C1072T	p.Q358X
exonic	*FBXW7*	uc003ims.3	c.G1818A	p.W606X
exonic	*GNB1*	uc001aif.3	c.T239C	p.I80T
exonic	*HIST1H1E*	uc003ngq.3	c.G236A	p.R79H
exonic	*HIST1H1E*	uc003ngq.3	c.C491T	p.A164V
exonic	*ID3*	uc001bhh.4	c.C190T	p.L64F
exonic	*ID3*	uc001bhh.4	c.191_195del	p.64_65del
exonic	*IKBKB*	uc003xov.3	c.A512G	p.K171R
exonic	*IKBKB*	uc011lcq.2	c.9_10insG	p.S3fs
exonic	*IKZF3*	uc002hsu.3	c.T485G	p.L162R
exonic	*IKZF3*	uc002hsu.3	c.T485G	p.L162R
exonic	*IKZF3*	uc002hsu.3	c.T485G	p.L162R
exonic	*IKZF3*	uc002hsu.3	c.T485G	p.L162R
exonic	*IKZF3*	uc002hsu.3	c.T485G	p.L162R
exonic	*IKZF3*	uc002hsu.3	c.T485G	p.L162R
exonic	*IKZF3*	uc002hsu.3	c.T485G	p.L162R
exonic	*IRF4*	uc003msz.4	c.C342A	p.S114R
splicing	*IRF4*		Chr6:393099,TGCAGAGCAGAGCGG>T	
exonic	*ITPKB*	uc001hqh.3	c.G868A	p.A290T
exonic	*KDM6A*	uc011mkz.2	c.G3813A	p.W1271X
exonic	*KRAS*	uc001rgp.1	c.G34A	p.G12S
exonic	*KRAS*	uc001rgp.1	c.G38A	p.G13D
exonic	*KRAS*	uc001rgp.1	c.G38A	p.G13D
exonic	*KRAS*	uc001rgp.1	c.A183C	p.Q61H
exonic	*KRAS*	uc001rgp.1	c.G35A	p.G12D
exonic	*KRAS*	uc001rgp.1	c.C64A	p.Q22K
exonic	*KRAS*	uc001rgp.1	c.G35A	p.G12D
exonic	*KRAS*	uc001rgp.1	c.G35A	p.G12D
exonic	*KRAS*	uc001rgp.1	c.G34T	p.G12C
exonic	*KRAS*	uc001rgp.1	c.A351T	p.K117N
splicing	*LTB*		Chr6:31549335,C>T	
exonic	*LTB*	uc003nul.3	c.C206T	p.A69V
exonic	*MAP2K1*	uc010bhq.3	c.G607A	p.E203K
exonic	*MED12*	uc004dyy.3	c.G97A	p.E33K
exonic	*MED12*	uc004dyy.3	c.G131A	p.G44D
exonic	*MED12*	uc004dyy.3	c.G97A	p.E33K
exonic	*MED12*	uc004dyy.3	c.T107G	p.L36R
exonic	*MED12*	uc004dyy.3	c.G131C	p.G44A
exonic	*MED12*	uc004dyy.3	c.G97A	p.E33K
exonic	*MED12*	uc004dyy.3	c.T107G	p.L36R
exonic	*MED12*	uc004dyy.3	c.G130A	p.G44S

exonic	*MED12*	uc004dyy.3	c.G97A	p.E33K
exonic	*MED12*	uc004dyy.3	c.G130C	p.G44R
exonic	*MED12*	uc004dyy.3	c.G130A	p.G44S
exonic	*MED12*	uc004dyy.3	c.95_97del	p.32_33del
exonic	*MGA*	uc010ucy.2	c.G4032A	p.W1344X
splicing	*MGA*		Chr15:42052728,G>T	
exonic	*MGA*	uc001zog.1	c.C2566T	p.Q856X
exonic	*MGA*	uc010ucy.2	c.G7307A	p.R2436H
exonic	*MGA*	uc001zog.1	c.A1918T	p.K640X
splicing	*MGA*		Chr15:42005696,T>C	
exonic	*MGA*	uc001zog.1	c.T581A	p.L194X
exonic	*MGA*	uc001zog.1	c.C2009A	p.S670X
exonic	*MGA*	uc010ucy.2	c.C7450T	p.Q2484X
exonic	*MGA*	uc010ucy.2	c.6857delA	p.E2286fs
exonic	*MGA*	uc001zog.1	c.552_553insA	p.N184fs
exonic	*MGA*	uc001zog.1	c.2666_2667insT	p.H889fs
exonic	*MGA*	uc001zog.1	c.2457delT	p.R819fs
exonic	*MGA*	uc001zog.1	c.2678_2679del	p.893_893del
exonic	*MGA*	uc010ucy.2	c.4065_4069del	p.1355_1357del
exonic	*MLL2*	uc001rta.4	c.C12844T	p.R4282X
exonic	*MLL2*	uc001rta.4	c.C1029G	p.Y343X
exonic	*MLL3*	uc003wla.3	c.C5371T	p.Q1791X
exonic	*MLL3*	uc003wla.3	c.6159_6160del	p.2053_2054del
exonic	*MYD88*	uc011ayj.2	c.T613C	p.X205R
exonic	*MYD88*	uc003chx.3	c.G649T	p.V217F
exonic	*MYD88*	uc003chx.3	c.G649T	p.V217F
exonic	*MYD88*	uc011ayj.2	c.T613C	p.X205R
exonic	*MYD88*	uc003chx.3	c.G649T	p.V217F
exonic	*MYD88*	uc003chx.3	c.C656G	p.S219C
exonic	*MYD88*	uc003chx.3	c.C656G	p.S219C
exonic	*MYD88*	uc011ayj.2	c.T613C	p.X205R
exonic	*NFKBIE*	uc003oxe.1	c.C887T	p.T296I
exonic	*NFKBIE*	uc003oxe.1	c.C782T	p.T261M
exonic	*NFKBIE*	uc003oxe.1	c.677delG	p.G226fs
exonic	*NFKBIE*	uc003oxe.1	c.1270_1271insATG	p.L424delinsML
exonic	*NFKBIE*	uc003oxe.1	c.759_762del	p.253_254del
exonic	*NFKBIE*	uc003oxe.1	c.759_762del	p.253_254del
exonic	*NFKBIE*	uc003oxe.1	c.759_762del	p.253_254del
exonic	*NFKBIE*	uc003oxe.1	c.759_762del	p.253_254del
exonic	*NFKBIE*	uc003oxe.1	c.759_762del	p.253_254del
exonic	*NFKBIE*	uc003oxe.1	c.759_762del	p.253_254del
exonic	*NFKBIE*	uc003oxe.1	c.759_762del	p.253_254del
exonic	*NFKBIE*	uc003oxe.1	c.759_762del	p.253_254del
exonic	*NFKBIE*	uc003oxe.1	c.759_762del	p.253_254del
exonic	*NFKBIE*	uc003oxe.1	c.759_762del	p.253_254del
exonic	*NFKBIE*	uc003oxe.1	c.819_825del	p.273_275del

exonic	*NOTCH1*	uc004chz.3	c.C7501T	p.Q2501X
exonic	*NOTCH1*	uc004chz.3	c.C7318T	p.Q2440X
exonic	*NOTCH1*	uc004chz.3	c.A6529T	p.K2177X
exonic	*NOTCH1*	uc004chz.3	c.C7459T	p.Q2487X
exonic	*NOTCH1*	uc004chz.3	c.C7183T	p.Q2395X
exonic	*NOTCH1*	uc004chz.3	c.G7378T	p.E2460X
exonic	*NOTCH1*	uc004chz.3	c.C7225T	p.Q2409X
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.6827_6831del	p.2276_2277del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7541_7542del	p.2514_2514del
exonic	*NOTCH1*	uc004chz.3	c.7207delC	p.Q2403fs
exonic	*NRAS*	uc009wgu.3	c.G34T	p.G12C
exonic	*NRAS*	uc009wgu.3	c.G436A	p.A146T

splicing	*PAX5*		Chr9:37033981,A>T	
exonic	*POT1*	uc003vlm.3	c.T126G	p.D42E
exonic	*POT1*	uc003vlm.3	c.A281G	p.Q94R
splicing	*POT1*		Chr7:124537267,C>A	
exonic	*POT1*	uc003vlm.3	c.A797T	p.H266L
exonic	*POT1*	uc003vlm.3	c.1072_1073insT	p.Q358fs
exonic	*POT1*	uc003vlm.3	c.1300_1301insA	p.V434fs
exonic	*POT1*	uc003vlm.3	c.1781_1782del	p.594_594del
exonic	*POT1*	uc003vlm.3	c.347delC	p.P116fs
exonic	*PRDM1*	uc003prd.2	c.A931C	p.K311Q
exonic	*PTPN11*	uc001ttx.3	c.T1504C	p.S502P
exonic	*PTPN11*	uc001ttw.1	c.G181T	p.D61Y
exonic	*PTPN11*	uc001ttw.1	c.A172T	p.N58Y
exonic	*RAD21*	uc003yod.3	c.1156_1161del	p.386_387del
exonic	*RB1*	uc001vcb.3	c.G610T	p.E204X
exonic	*RB1*	uc001vcb.3	c.21delA	p.R7fs
exonic	*RB1*	uc001vcb.3	c.14delC	p.T5fs
exonic	*RB1*	uc001vcb.3	c.1472_1473del	p.491_491del
exonic	*ROBO1*	uc003dqe.2	c.A4387T	p.K1463X
exonic	*ROBO1*	uc003dqe.2	c.C3814T	p.Q1272X
exonic	*SAMHD1*	uc002xgh.2	c.G348T	p.K116N
splicing	*SAMHD1*		Chr20:35545124,C>A	
exonic	*SAMHD1*	uc002xgh.2	c.T861A	p.Y287X
splicing	*SAMHD1*		Chr20:35533766,C>T	
exonic	*SAMHD1*	uc002xgh.2	c.A346T	p.K116X
splicing	*SAMHD1*		Chr20:35545124,C>T	
exonic	*SAMHD1*	uc002xgh.2	c.453_454insG	p.G151fs
exonic	*SAMHD1*	uc002xgh.2	c.646_647del	p.216_216del
exonic	*SAMHD1*	uc002xgh.2	c.16_17insCC	p.S6fs
exonic	*SAMHD1*	uc002xgh.2	c.646_647del	p.216_216del
splicing	*SETD2*		Chr3:47155365,C>G	
exonic	*SETD2*	uc003cqs.3	c.T2415A	p.C805X
exonic	*SETD2*	uc003cqv.3	c.6299delA	p.K2100fs
exonic	*SETD2*	uc003cqs.3	c.3460_3463del	p.1154_1155del
exonic	*SF3B1*	uc002uue.3	c.G2225A	p.G742D
exonic	*SF3B1*	uc002uue.3	c.G2225A	p.G742D
exonic	*SF3B1*	uc002uue.3	c.G2225A	p.G742D
exonic	*SF3B1*	uc002uue.3	c.G2225A	p.G742D
exonic	*SF3B1*	uc002uue.3	c.G2223C	p.K741N
exonic	*SF3B1*	uc002uue.3	c.A2222C	p.K741T
exonic	*SF3B1*	uc002uue.3	c.G2225A	p.G742D
exonic	*SF3B1*	uc002uue.3	c.A2222C	p.K741T
exonic	*SF3B1*	uc002uue.3	c.G2225A	p.G742D
exonic	*SF3B1*	uc002uue.3	c.G2225A	p.G742D
exonic	*SF3B1*	uc002uue.3	c.G2225A	p.G742D
exonic	*SF3B1*	uc002uue.3	c.G2225A	p.G742D

exonic	*SF3B1*	uc002uue.3	c.T2111A	p.I704N
exonic	*SF3B1*	uc002uue.3	c.G2219A	p.G740E
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.A2110T	p.I704F
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.G1998T	p.K666N
exonic	*SF3B1*	uc002uue.3	c.C1986A	p.H662Q
exonic	*SF3B1*	uc002uue.3	c.C1984G	p.H662D
exonic	*SF3B1*	uc002uue.3	c.G1874A	p.R625H
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.A1868G	p.Y623C
exonic	*SF3B1*	uc002uue.3	c.G1866T	p.E622D
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.A1997C	p.K666T
exonic	*SF3B1*	uc002uue.3	c.C1873T	p.R625C
exonic	*SF3B1*	uc002uue.3	c.A2681G	p.D894G
exonic	*SF3B1*	uc002uue.3	c.C1986G	p.H662Q
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.G1998C	p.K666N
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.T2111A	p.I704N
exonic	*SF3B1*	uc002uue.3	c.G2219A	p.G740E
exonic	*SF3B1*	uc002uue.3	c.C1986A	p.H662Q
exonic	*SF3B1*	uc002uue.3	c.C1984G	p.H662D
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.G1866T	p.E622D
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.A1997C	p.K666T
exonic	*SF3B1*	uc002uue.3	c.G2219A	p.G740E
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SF3B1*	uc002uue.3	c.A2098G	p.K700E
exonic	*SH2B3*	uc001tsf.3	c.C1386A	p.Y462X
exonic	*SMC5*	uc004ahr.2	c.C2116T	p.Q706X
exonic	*SMC5*	uc004ahr.2	c.2066delA	p.E689fs
exonic	*SP140*	uc002vql.3	c.1939delG	p.G647fs
exonic	*SP140*	uc002vqk.2	c.970delG	p.G324fs
exonic	*SP140*	uc002vql.3	c.1316_1317insTAAT	p.D439fs
exonic	*SPEN*	uc001axk.1	c.G6416C	p.S2139T
exonic	*SPEN*	uc001axk.1	c.C1882T	p.Q628X
exonic	*SPEN*	uc001axk.1	c.3441_3442del	p.1147_1148del
exonic	*SPEN*	uc001axk.1	c.3552_3553del	p.1184_1185del
exonic	*SPEN*	uc001axk.1	c.3703_3731del	p.1235_1244del

exonic	*SPEN*	uc001axk.1	c.3973_3977del	p.1325_1326del
exonic	*SPEN*	uc001axk.1	c.6762delG	p.Q2254fs
exonic	*TET2*	uc011cez.2	c.C4456T	p.R1486X
exonic	*TET2*	uc011cez.2	c.C2950T	p.Q984X
exonic	*TET2*	uc011cez.2	c.4532delA	p.E1511fs
exonic	*TET2*	uc011cez.2	c.3417delT	p.N1139fs
exonic	*TET2*	uc011cez.2	c.3961delT	p.F1321fs
exonic	*TET2*	uc011cez.2	c.3961delT	p.F1321fs
exonic	*TET2*	uc011cez.2	c.4618delG	p.G1540fs
exonic	*TP53*	uc010vug.2	c.G556A	p.V186I
exonic	*TP53*	uc002gig.1	c.T695C	p.I232T
splicing	*TP53*		Chr17:7578370,C>T	
splicing	*TP53*		Chr17:7579311,C>A	
exonic	*TP53*	uc002gig.1	c.C413T	p.A138V
splicing	*TP53*		Chr17:7579311,C>A	
exonic	*TP53*	uc002gih.3	c.G841A	p.D281N
exonic	*TP53*	uc002gig.1	c.A641G	p.H214R
exonic	*TP53*	uc002gig.1	c.T714A	p.C238X
splicing	*TP53*		Chr17:7579311,C>A	
exonic	*TP53*	uc002gig.1	c.T752G	p.I251S
exonic	*TP53*	uc002gig.1	c.G542C	p.R181P
exonic	*TP53*	uc002gih.3	c.C817T	p.R273C
exonic	*TP53*	uc002gih.3	c.G818C	p.R273P
splicing	*TP53*		Chr17:7577610,T>C	
exonic	*TP53*	uc002gig.1	c.A659G	p.Y220C
exonic	*TP53*	uc002gig.1	c.A488C	p.Y163S
exonic	*TP53*	uc002gig.1	c.A707G	p.Y236C
exonic	*TP53*	uc002gig.1	c.A701G	p.Y234C
exonic	*TP53*	uc002gig.1	c.A763T	p.I255F
exonic	*TP53*	uc002gig.1	c.G646A	p.V216M
exonic	*TP53*	uc002gih.3	c.G811A	p.E271K
exonic	*TP53*	uc002gig.1	c.C493T	p.Q165X
exonic	*TP53*	uc002gig.1	c.A488G	p.Y163C
exonic	*TP53*	uc002gig.1	c.G427A	p.V143M
exonic	*TP53*	uc002gig.1	c.G711C	p.M237I
exonic	*TP53*	uc002gig.1	c.T379A	p.S127T
exonic	*TP53*	uc002gig.1	c.A704G	p.N235S
splicing	*TP53*		Chr17:7579310,A>C	
exonic	*TP53*	uc002gih.3	c.A838G	p.R280G
exonic	*TP53*	uc002gih.3	c.T823C	p.C275R
exonic	*TP53*	uc002gig.1	c.A736G	p.M246V
exonic	*TP53*	uc002gig.1	c.G469T	p.V157F
exonic	*TP53*	uc002gih.3	c.G841C	p.D281H
exonic	*TP53*	uc002gig.1	c.G527C	p.C176S
exonic	*TP53*	uc002gig.1	c.A707G	p.Y236C
exonic	*TP53*	uc002gig.1	c.A707G	p.Y236C

exonic	*TP53*	uc002gig.1	c.T645G	p.S215R
exonic	*TP53*	uc010cnk.1	c.C417A	p.C139X
exonic	*TP53*	uc002gig.1	c.A536G	p.H179R
exonic	*TP53*	uc002gij.2	c.C1024T	p.R342X
exonic	*TP53*	uc002gig.1	c.G713T	p.C238F
exonic	*TP53*	uc002gih.3	c.A955T	p.K319X
exonic	*TP53*	uc002gig.1	c.G733C	p.G245R
exonic	*TP53*	uc002gig.1	c.A536G	p.H179R
splicing	*TP53*		Chr17:7576927,C>G	
exonic	*TP53*	uc010cnk.1	c.261delC	p.P87fs
exonic	*TP53*	uc010cnk.1	c.232_233insA	p.A78fs
exonic	*TP53*	uc002gig.1	c.601_602insA	p.L201fs
exonic	*TP53*	uc002gig.1	c.456_457insC	p.P152fs
exonic	*TP53*	uc002gig.1	c.721delT	p.S241fs
exonic	*TP53*	uc002gig.1	c.417delG	p.K139fs
exonic	*TP53*	uc010cnk.1	c.410_411del	p.137_137del
exonic	*TP53*	uc002gig.1	c.626_627del	p.209_209del
exonic	*TP53*	uc002gig.1	c.652_654del	p.218_218del
exonic	*TP53*	uc002gig.1	c.566_581del	p.189_194del
exonic	*TP53*	uc002gij.2	c.1028delA	p.E343fs
exonic	*TP53*	uc002gih.3	c.847_848insAGCCCGG	p.R283fs
exonic	*TP53*	uc002gig.1	c.706_707insAC	p.Y236fs
exonic	*TP53*	uc002gig.1	c.649_650insCATAGTGTG	p.V217delinsHSVV
exonic	*TP53*	uc002gig.1	c.463_474del	p.155_158del
exonic	*TRAF3*	uc001ymd.2	c.A1276T	p.K426X
exonic	*TRAF3*	uc001ymd.2	c.431delA	p.E144fs
exonic	*TRAF3*	uc001ymd.2	c.1503delG	p.Q501fs
exonic	*TRAF3*	uc001ymd.2	c.203delG	p.C68fs
exonic	*TRAF3*	uc001ymd.2	c.1670_1673del	p.557_558del
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711C	p.E571Q
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K

exonic	*XPO1*	uc002sbj.3	c.G1711C	p.E571Q
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.A1871G	p.D624G
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.A1712G	p.E571G
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*XPO1*	uc002sbj.3	c.G1711A	p.E571K
exonic	*ZMYM3*	uc004dzh.2	c.T261A	p.Y87X
splicing	*ZMYM3*		ChrX:70467361,C>T	
exonic	*ZMYM3*	uc004dzh.2	c.C964T	p.Q322X
exonic	*ZMYM3*	uc004dzh.2	c.C581A	p.S194X
exonic	*ZMYM3*	uc004dzh.2	c.1700_1701insT	p.Y567fs
exonic	*ZMYM3*	uc004dzh.2	c.3660delT	p.F1220fs
exonic	*ZMYM3*	uc004dzh.2	c.1538_1539del	p.513_513del
splicing	*ZRSR2*		ChrX:15822233,G>C	
exonic	*ZRSR2*	uc004cxg.4	c.C868T	p.R290X
splicing	*ZRSR2*		ChrX:15836766,G>A	

Table S4. Likelihood of overall response according to therapy received, previous treatment status and FISH/mutational abnormalities

	Lenalidomide Monotherapy						**Lenalidomide Combination Therapy**					
	Treatment-naïve			**Relapsed/Refractory**			**Treatment-naïve**			**Relapsed/Refractory**		
	OR	**95% CI**	**p**	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Del(17p)	**0.118**	**0.012-1.126**	**0.070**	**0.172**	**0.008-3.618**	**0.251**	**0.333**	**0.012-8.995**	**1.000**	**0.308**	**0.125-0.760**	**0.014**
Del(11q)	**0.347**	**0.089-1.351**	**0.179**	**0.833**	**0.203-3.422**	**1.000**	**0.062**	**0.003-1.414**	**0.067**	**0.660**	**0.280-1.553**	**0.374**
Tri(12)	**0.722**	**0.173-3.019**	**0.724**	**1.600**	**0.325-7.888**	**0.689**	**2.273**	**0.101-50.911**	**1.000**	**0.680**	**0.245-1.891**	**0.586**
Del(13p)	**1.829**	**0.505-6.615**	**0.515**	**1.100**	**0.284-4.256**	**1.000**	**0.172**	**0.008-3.818**	**0.232**	**0.700**	**0.301-1.628**	**0.529**
TP53	**0.159**	**0.016-1.573**	**0.150**	**0.059**	**0.003-1.121**	**0.012**	**0.432**	**0.017-10.888**	**1.000**	**0.260**	**0.101-0.675**	**0.008**
Complex Karyotype	**2.571**	**0.235-28.089**	**0.613**	**0.667**	**0.106-4.182**	**1.000**	**0.094**	**0.005-1.909**	**0.207**	**0.255**	**0.094-0.692**	**0.009**
ATM	**0.140**	**0.006-3.120**	**0.187**	**0.410**	**0.016-10.692**	**1.000**	**1.479**	**0.069-31.733**	**1.000**	**1.476**	**0.292-7.461**	**1.000**
KRAS	**0.248**	**0.010-6.465**	**0.439**	**1.286**	**0.024-68.082**	**1.000**	**0.020**	**0.001-0.615**	**0.067**	**0.258**	**0.041-1.610**	**0.147**
MGA	**2.467**	**0.095-64.203**	**1.000**	**0.234**	**0.011-5.214**	**0.495**	**0.432**	**0.017-10.888**	**1.000**	**0.221**	**0.050-0.977**	**0.046**
SF3B1	**2.222**	**0.377-13.082**	**0.438**	**0.134**	**0.015-1.221**	**0.106**	**1.479**	**0.069-31.733**	**1.000**	**0.536**	**0.187-1.536**	**0.260**
DDX3X	**0.787**	**0.015-41.586**	**1.000**	**0.234**	**0.011-5.214**	**0.495**	**0.082**	**0.001-4.816**	**1.000**	**0.041**	**0.002-0.785**	**0.006**

Figure S1. Box plot of the mutational burden comparing unmutated IGHV to mutated IGHV patients.

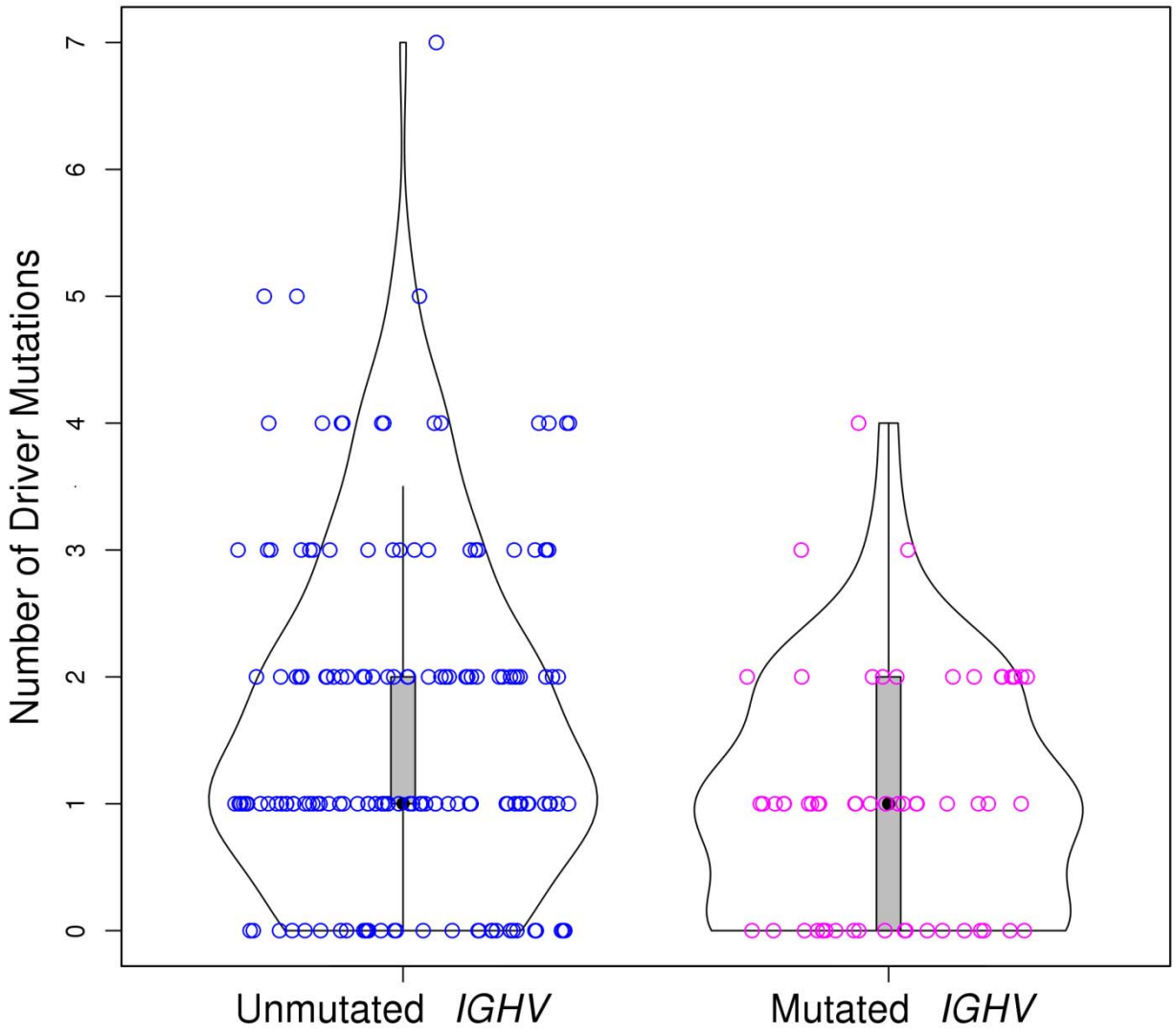
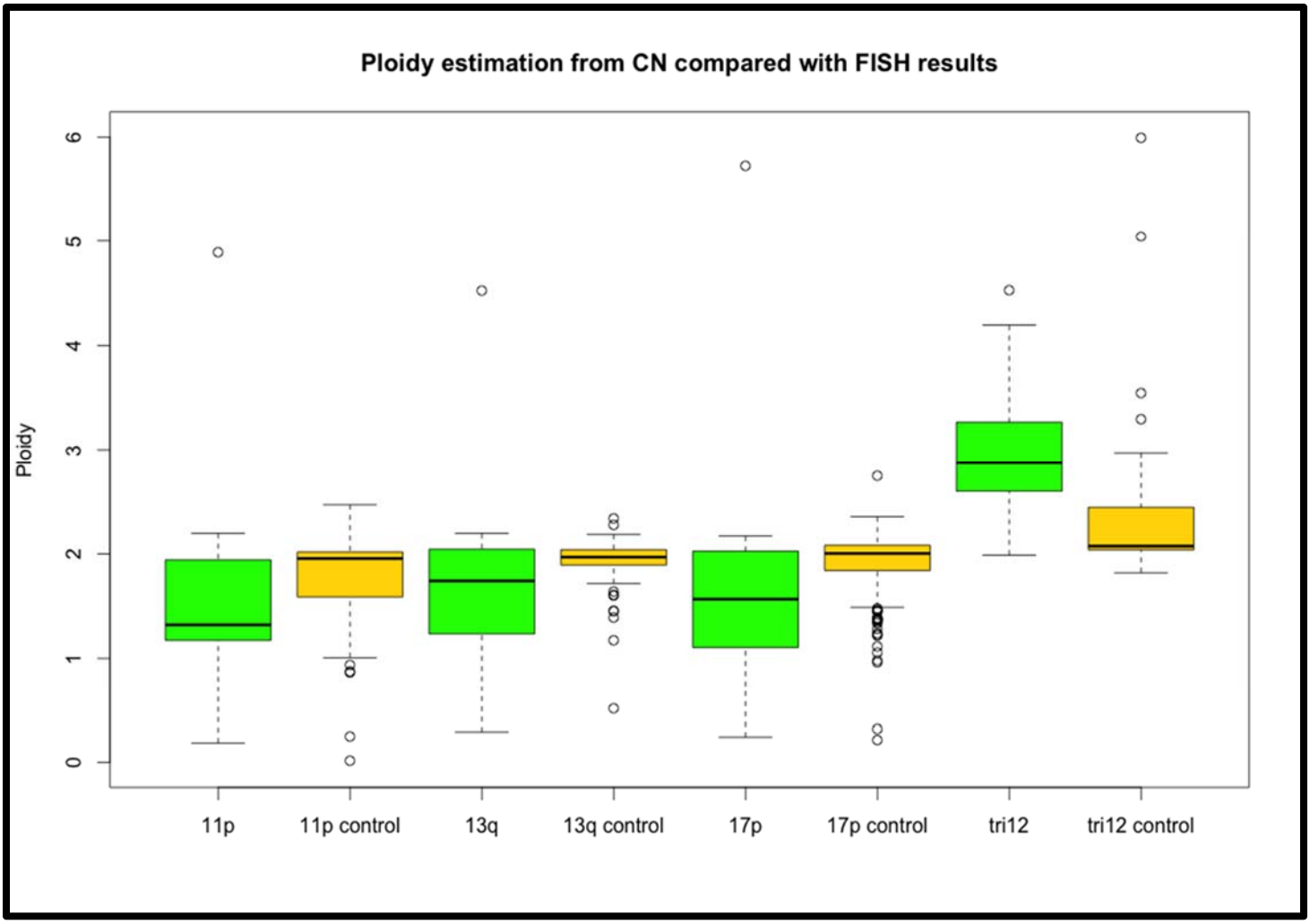


Figure S2. Concordance between FISH results and ploidy estimations from copy number predictions within our analysis.



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