**Supplementary Design and Methods** Primers for fluorescent fragment PCR (FF-PCR) and sanger sequencing (forward primer indicated first)

| Locus | FF-PCR | Sanger |
|---|---|---|
| NR21 | TAAATGTATGTCTCCCCTGG<br>Hex-ATTCCTACTCCGCATTCACA | |
| NR22 | GAGGCTTGTCAAGGACATAA<br>Fam-AATTCGGATGCCATCCAGTT | |
| NR24 | CCATTGCTGAATTTTACCTC<br>Hex-GAGGCTTGTCAAGGACATAA | |
| BAT25 | Tmr-TCGCCTCCAAGAATGTAAGT<br>TCTGCATTTTAACTATGGCTC | |
| BAT26 | AACCATTCAACATTTTTAACCC<br>Fam-TGACTACTTTTGACTTCAGCC | |
| MONO27 | TTGCAGTGAGCTGAGATTGC<br>Fam-GGTGGATCAAATTTCACTTGG | |
| ATR | ACGGACATGTGGACCTCTTC<br>TCACTCACCAAGTTTTACTGGA | TCTTCCTCCGTGAGTCCTGT<br>CTGAGGAAGAGCAGCCCATA |
| ATM | AAATCCTTTTTCTGTATGGGAT<br>GTTACTGAGTCTAAAACATGG | CTCAGCAACAGTGGTTAG<br>GATATGATTTAGACCTGAAGAG |
| BLM | CTCTGCCACCAGGAAGAATC<br>CAGCAGTGCTTGTGAGAACA | CTCTGCCACCAGGAAGAATC<br>GGAAGATTTGCTGGCTGCTA |
| CHK1 | ATGGGACCAACCCAGTGAC<br>TCCAAGAAATCGGTACTCTTTCA | CCTCCCAAAGTGCTGTGATT<br>TCCAAGAAATCGGTACTCTTTCA |
| CtIP | TTGTCCCCTTCTCTTTTACAGC<br>CCCAAGACTGTGATGTGTGAA | TTGTCCCCTTCTCTTTTACAGC<br>GGGGCAGCTTACTTCATGTT |
| DNA-PKcs | TGGAGCAATGATGTAAGAGCTG<br>AAATAGCAGGCTGTGCCAGT | |
| BRCA1 | CAGGTTTAATATCCACTTTG<br>ATTAGTTCTGATTTTTGGTC | |
| BRCA2 Exon 9 | GATACAGAATTTATCATCTTG<br>CTGAAAATTACAATGAAAGG | |
| BRCA2 Exon 22 | GATACAGAATTTATCATCTTG<br>CTGAAAATTACAATGAAAGG | |
| MRE11 | TGGAGGAGAATCTTAGGGAAAA<br>AATTGAAATGTTGAGGTTGCC | TTGAAATGAATTGTCGCCTATG<br>AATTGAAATGTTGAGGTTGCC |
| PTEN | AGTTCCCTCAGCCGTTACCT<br>TTTTGGATATTTCTCCCAATGAA | TGCAGATCCTCAGTTTGTGG<br>GCCATAAGGCCTTTTCCTTC |
| PARP1 | CGCACATCTTGTCCCCTTGG<br>GGCCCTCACCTTCCTCCTTG | |
| TNK1 | AACCATTGTTTCATTGACA<br>AATCTTACCAGTGCTGTTTC | |
| RAD50 | TGCGACTTGCTCCAGATAAA<br>GCTACATGTACAGTGAAGGTAAATCC | CTCTGCCACCAGGAAGAATC<br>GGAAGATTTGCTGGCTGCTA |
| TGF-βII | CAAGCTCCCCTACCATGACT<br>TGCACTCATCAGAGCTACAGG | |

**TP53 sequencing** *TP53* (NC_000017-9) mutations were analyzed from DNA using the Roche GS FLX sequencing platform (Roche, Indianapolis, IN) as described previously[1]. We sequenced 14 amplicons for 95 samples across the entire *TP53* coding region and untranslated exon 1. Patient-specific barcodes, adapted to polymerase chain reaction primers in the second round of amplification were derived from the Roche GS Titanium protocol (Roche). Average sequencing coverage across *TP53* was around 1,200× and > 99% of the sequenced amplicons had sequence coverage of > 100×. This allowed reliable detection of mutant clones down to 1% to 2% relative mutation abundance (RMA), defined as the proportion of sequence reads containing the mutation. Independent polymerase chain reaction and GS FLX sequencing experiments were performed for confirmation of mutations in all cases (giving > 2,000× total coverage on average across a given mutation). These experiments also negated sampling errors for RMA calculations that were due to a higher combined sequencing coverage. Sanger sequencing confirmation was performed in a selection of patients where the mutation had an RMA of ≥ 25%. To determine the presence of low-abundance mutant clones, two samples were re-sequenced at greater depth (2,500× *v* 1,200×).

| | |
|---|---|
| p53promoterA_F | GTAGTGCGATGGCCAGTCAGAGTGATAAGGGTTGTGAAGG |
| p53promoterA_R | CAGTGTGCAGCGATGACCTGGCACAAAGCTGGACAGT |
| p53promoterB/exoF | GTAGTGCGATGGCCAGTGGCGGATTACTTGCCCTTAC |
| p53promoterB/exoR | CAGTGTGCAGCGATGACCGAGAGCCCGTGACTCAG |
| p53exon2_F | GTAGTGCGATGGCCAGTCTGGATCCCCACTTTTCCTC |
| p53exon2_R | CAGTGTGCAGCGATGACTCCCACAGGTCTCTGCTAGG |
| p53exon3_F | GTAGTGCGATGGCCAGTAGCGAAAATTCATGGGACTG |
| p53exon3_R | CAGTGTGCAGCGATGACGGGGACTGTAGATGGGTGAA |
| p53exon4A_F | GTAGTGCGATGGCCAGTCCTGGTCCTCTGACTGCTCT |
| p53exon4A_R | CAGTGTGCAGCGATGACTTCTGGGAAGGGACAGAAGA |
| p53exon4B_F | GTAGTGCGATGGCCAGTGTCCAGATGAAGCTCCCAGA |
| p53exon4B_R | CAGTGTGCAGCGATGACCAGGCATTGAAGTCTCATGG |
| p53exon5_F | GTAGTGCGATGGCCAGTTTTCAACTCTGTCTCCTTCCTCTT |
| p53exon5_R | CAGTGTGCAGCGATGACAGCCCTGTCGTCTCTCCAG |
| p53exon6_F | GTAGTGCGATGGCCAGTCAGGCCTCTGATTCCTCACT |
| p53exon6_R | CAGTGTGCAGCGATGACCTTAACCCCTCCTCCCAGAG |
| p53exon7_F | GTAGTGCGATGGCCAGTTCATCTTGGGCCTGTGTTATC |
| p53exon7_R | CAGTGTGCAGCGATGACAGTGTGCAGGGTGGCAAG |
| p53exon8_F | GTAGTGCGATGGCCAGTGCCTCTTGCTTCTCTTTTCC |
| p53exon8_R | CAGTGTGCAGCGATGACTAACTGCACCCTTGGTCTCC |
| p53exon9_F | GTAGTGCGATGGCCAGTGGAGACCAAGGGTGCAGTTA |
| p53exon9_R | CAGTGTGCAGCGATGACGAAAACGGCATTTTGAGTGTT |
| p53exon10_F | GTAGTGCGATGGCCAGTACTTCTCCCCCTCCTCTGTT |
| p53exon10_R | CAGTGTGCAGCGATGACGAAGGCAGGATGAGAATGGA |
| p53exon11_F | GTAGTGCGATGGCCAGTTGTCATCTCTCCTCCCTGCT |

| | |
|---|---|
| p53exon11_R | CAGTGTGCAGCGATGACCAAGGGTTCAAAGACCCAAA |
| p53extraexons_F | GTAGTGCGATGGCCAGTAACTTCAGAACACCAACTTATACCA |
| p53extraexons_R | CAGTGTGCAGCGATGACAGGTGTATTAAATCCATTTTCAACTT |

**Cell Culture** The leukemic cell lines; HL60, K562, NB4, U937, KG-1, Raji, Molm-13 and SD-1 cells were obtained from the American Type Culture Collection (ATCC). The colon cancer cell lines: DLD-1, LoVo, HCT116 and the leukemic cell lines, OCI-AML3, REH, OCI-AML3 were obtained from the DSMZ, Braunschweig, Germany. The myelomonocytic/myelodysplastic cell line, P39 was kindly donated by Richard Darley, (University of Wales, Cardiff, UK). Retrovirally immortalized PD220Di (human FANCD2$^{-/-}$) was purchased from the Coriell Institute for Medical Research, Camden, NJ, USA. These cell lines were purchased within the last five years, propagated, expanded, and frozen immediately into numerous aliquots after arrival. The cells revived from the frozen stock were used within 10–20 passages, not exceeding a period of 2–3 months. The ATCC and DSMZ use morphological, cytogenetic and DNA profile analysis for characterization of cell lines. Prior to the study start, all MDS/AML cell lines were subjected to genotyping and mutation analysis for authenticity compared to the genotype characterised by the ATCC and DSMZ. Leukemic cell lines were cultured at 37°C (5% $CO_2$) in Dutch-modified, RPMI 1640 medium, supplemented with 10% fetal calf serum, 4mM glutamine and 1% penicillin/streptomycin (all purchased from Sigma-Aldrich Co. Ltd. Poole, UK). Colon cancer cell lines were cultured in Dulbecco's minimal essential medium (DMEM) supplemented with 10% (v/v) fetal calf serum, 4mM glutamine and 1% penicillin/streptomycin. All cell lines were early passaged (between 10-20 passages). Peripheral blood lymphocytes (PBL) from unnamed normal subjects were prepared from heparinized blood using Hypaque-Ficoll (Sigma) gradients and cultured at 1 x $10^6$ cells/ml in RPMI 1640, supplemented with 10% (v/v) fetal calf serum, 4mM glutamine and 1% penicillin/streptomycin. PBL were stimulated by adding phytohemagluttinin (PHA, Sigma) for 48 h, washed several times to remove PHA and then cultured in 1U/ml of Interleukin-2 (IL-2) for a maximum of 14 days. For primary cell cultures, bone marrow aspirates were taken from AML patients. Mononuclear cells were extracted using Hypaque-Ficoll (Sigma) gradients and cultured at 1 x $10^6$ cells/ml in RPMI 1640, supplemented with 20% (v/v) fetal calf serum, 4 mM glutamine, 1% penicillin/streptomycin, 10 ng/ml Il-3, 10 ng/ml IL-6 and 20 ng/ml stem cell factor (SCF). DNA was extracted from cell lines and from primary cells using the QIAamp DNA Blood Mini Kit (Qiagen).

**Single nucleotide polymorphism analysis (SNP-A)** High quality genomic DNA was digested with NspI and StyI restriction endonucleases, followed by ligation to an enzyme specific adaptor. The ligated product was amplified by PCR, fragmented and end labelled with biotin. The labelled product was then hybridized to a SNP6 microarray. The Affymetrix 450 fluidics station and the Affymetrix 3000 G7 gene scanner were used to wash, stain, and scan the arrays. Arrays were quality checked to achieve a CpC score

>1.7/batch and a MAPD of <0.3 and were genotyped using the Affymetrix Genotyping Console with the Birdseed v2.0 algorithm. The base line reference for copy number data was derived from a cohort of 91 normal controls consisting of cases from the Medical Clinics at King's College London, as well as by external, publicly available data. Significant genomic changes were identified by size selection and by overlap with known copy number variants obtained from the Database of Genomic Variants (DGV). Deletions >270Kb, gains >500Kb and copy neutral LOH (CN-LOH)/uniparental disomy (UPD) >6.9Mb with <50% overlap with copy number variations from the DGV were considered to be somatic aberrations and were included in the analysis. Loss of heterozygosity was analyzed with the Copy Number Analyzer for the Affymetrix GeneChip Mapping (CNAG ver 3.0) algorithm and the Partek software. We confirmed allele specific analysis, somatic abnormalities and also detection of homozygous regions of deletions by the parallel analysis of buccal DNA from the same individuals.

**Sanger Sequencing** PCR reactions contained 100 nM primer in Amplitaq 360 taq polymerase/buffer and 10 ng of DNA. PCR was performed using the following conditions: denaturation at 94°C for 10 min, 35 cycles of denaturation 94°C for 30 sec, annealing at 55°C for 30 sec and extension at 72°C for 30 sec. There was a final extension step of 72°C for 7 min. PCR products were gel excised and DNA extracted. Sequencing was performed using Big dye (ABI) as per manufacturer's instructions.

**Cell cycle analysis** PARPi were added to log phase cells. At 120 h after PARPi addition, aliquots of 2 X $10^5$ cells were taken and centrifuged at 400 g for 10 min. The supernatant was aspirated and then 70% (v/v) ethanol (at -20° C) was added to the cells and gently vortexed. The cell suspension was again centrifuged at 400xg for 10 min. The supernatant was aspirated and then 1 ml of staining solution (PBS plus 5 ng FITC, 40 µg propidium iodide, 500 µg RNAse) was added. Samples were analyzed using the FACScan flow cytometer (Becton Dickinson, Franklin Lakes, NJ). Calculating the percentage sub-$G_1$ events as a fraction of the total events derived the apoptotic index.

**PARP activity assay** MDS/AML cells were assessed for their intrinsic PARP activity by measuring the amount of poly(ADP-ribose) (PAR) synthesised by maximally stimulated PARP in a 6 min reaction, using a validated PARP activity assay[2]. Briefly, cells were washed in ice-cold PBS before permeabilising with digitonin (0.15 mg/mL, Sigma Aldrich, Dorset, UK). Confirmation of cell permeabilisation, and cell counting was performed using a haemocytometer following trypan blue staining. A known number of cells in reaction buffer (100 mM Tris-HCl, 120 mM $MgCl_2$, pH 7.8) were then exposed to blunt-ended oligonucleotide (10 µg/mL, 5' CGGAATTCCG 3') (Europrim, Invitrogen, Paisley, UK) in the presence of $NAD^+$ (350 µM, Sigma Aldrich,) at a final volume of 100 µl for 6 min at 26°C. Cells were then fixed onto a nitrocellulose membrane (Hybond-N, Amersham, GE Healthcare Life Sciences, Bucks, UK) and PAR detected using the mouse monoclonal anti-PAR 10H antibody (1.5 mg/mL, Prof. Alex Burkle, University Konstanz, Konstanz, Germany). Anti-PAR antibody was detected by using the goat polyclonal horseradish peroxidase-conjugated anti-mouse antibody (DAKO, Cambridgeshire, UK). Antibodies were diluted at a concentration of 1:1000 in blocking

buffer (phosphate-buffered saline, 0.05 % Tween 20 and 5 % milk powder). Final detection of the secondary antibody was carried out by developing with ECL detection fluid (Amersham) and chemiluminscent detection using the Fujifilm LAS 300 imager (Raytest, Sheffield, UK). PARP activity of untreated control cells was set as 100 % and activity in all PARPi treated samples was expressed as a percentage of these cells activity.

**Comparison of PARPi** Abrogation of PARP activity was quantified using a modified version of the PARP Universal Colorimetric Assay Kit (R & D Systems Ltd, Abingdon, UK). This assay measures the incorporation of biotinylated ADP-ribose onto histone proteins bound to a 96-well plate. Detection is made by streptavidin conjugated HRP, followed by the addition of an HRP substrate. In this case, nuclear extract from the MDS/AML cell line, U937 was used as a source of PARP enzyme. Increasing concentrations of different PARPi were incubated with the U937 cells in culture before nuclear extracts were prepared and tested for PARP activity.

**Annexin V staining** Annexin V staining by FACS analysis was used as a marker of apoptosis. Five days (120 h) after PARPi exposure, cells were incubated with anti-annexin V-FITC and propidium iodide and analyzed by FACS immediately. Using Annexin V-FITC (FL-1, X-axis) and propidium iodide (PI) (FL-2, Y-axis), the percentage of non-apoptotic (bottom left quadrant), early (bottom right quadrant) and late apoptotic cells (top right quadrant) could be determined.

**ELISA** The method is based on the protocol provided by Abcam (Cambridge, UK). 2 X $10^6$ cells were aspirated and washed in ice-cold PBS before lysis in extraction buffer (100 mM Tris, pH 7.4, 1 mM EGTA, 150 mM NaCl, 1 mM EDTA, 1% Triton X-100, 0.5% Sodium deoxycholate). Typically protein concentration was between 1-2mg/ml. All extracts were adjusted to 1mg/ml before assay. 100µl of cell extract was added to the wells of a 96 well plate and incubated at 4°C overnight. The extracts were washed 3 times with 200 µl PBS. The plates were then blocked in 200 µl blocking buffer, (5% non-fat dry milk or 5% serum in /PBS, per well) for 1 h. Then 100 µl of diluted primary antibody (1:50 for CtIP) was added to each well and incubated overnight at 4°C. The plates were again washed in PBS X5, before the addition of 100 µl of goat anti-rabbit IgG-HRP secondary antibody, diluted 1:1000) and incubated for 2h at at room temperature. The plates were then washed four times in PBS. Detection was made by the addition of 50 µl TMB (3,3',5,5'-tetramethylbenzidine) for 15-30 min and adding an equal volume of stopping solution (2 M $H_2SO_4$) before reading the optical density at 450 nm. A standard curve was prepared of relative absorbance vs protein concentration dependent on increasing concentration of si-RNA.

**Gene expression profiling** Total RNA was extracted from K562 cells transfected with Si-RNA targeted to CtIP, K562 transfected with CtIP over-expressing plasmid, pZGFP-C1-CtIP or Si-RNA scrambled oligonucleotide control using a hybrid TRIZOL (Invitrogen)/RNeasy (Qiagen) method. Briefly, cells were lysed and homogenized in 1 ml Trizol at room temperature for 5 min followed by phase separation by addition of 200 µl of chloroform. The aqueous phase was collected and an equal volume of 70% ethanol added, followed by application of this mixture to an RNeasy column. Subsequent steps

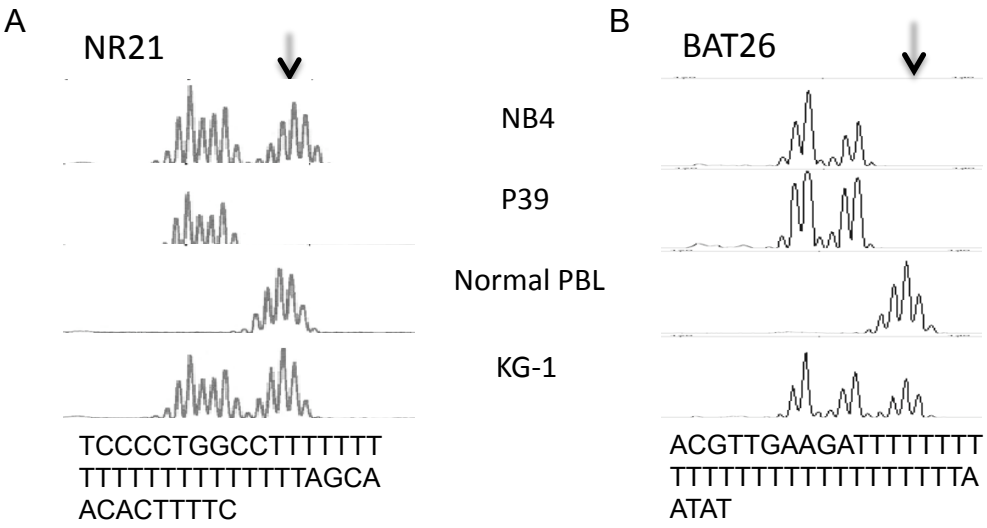
were according to manufacturer's instructions (Qiagen, Hilden, Germany). RNA quality was assessed using spectrophotometric measurement with the Nanodrop 8000 (Labtech International) and Agilent Bioanalyser (Agilent, Santa Clara, CA). Total RNA (200 ng) was processed using the Applause-WT plus and the Encore Biotin module (NuGen, San Carlos, CA). Quality control of the amplified product was performed using the Nanodrop spectrophotometer and Agilent Bioanalyser. The amplified product was fragmented and labelled using the Encore Biotin module kit. All procedures strictly adhered to the manufacturers protocols. The labelled products were hybridized to GeneChip Exon WT arrays (Affymetrix, Santa Clara, CA). The Affymetrix 450 fluidics station and the Affymetrix 3000 G7 gene scanner were used to wash, stain and scan the arrays. Cell intensity calculation, scaling and quality control were performed using Affymetrix Expression Console. Statistical analysis and gene lists were generated using Partek Express (Partek, St.Louis. MI).

## References

1. Jädersten M, Saft L, Smith A, Kulasekararaj A, Pomplun S, Göhring G, Hedlund A, Hast R, Schlegelberger B, Porwit A, Hellström-Lindberg E, Mufti GJ. TP53 mutations in low-risk myelodysplastic syndromes with del(5q) predict disease progression. *J Clin Oncol.* 2011;29:1971-9.

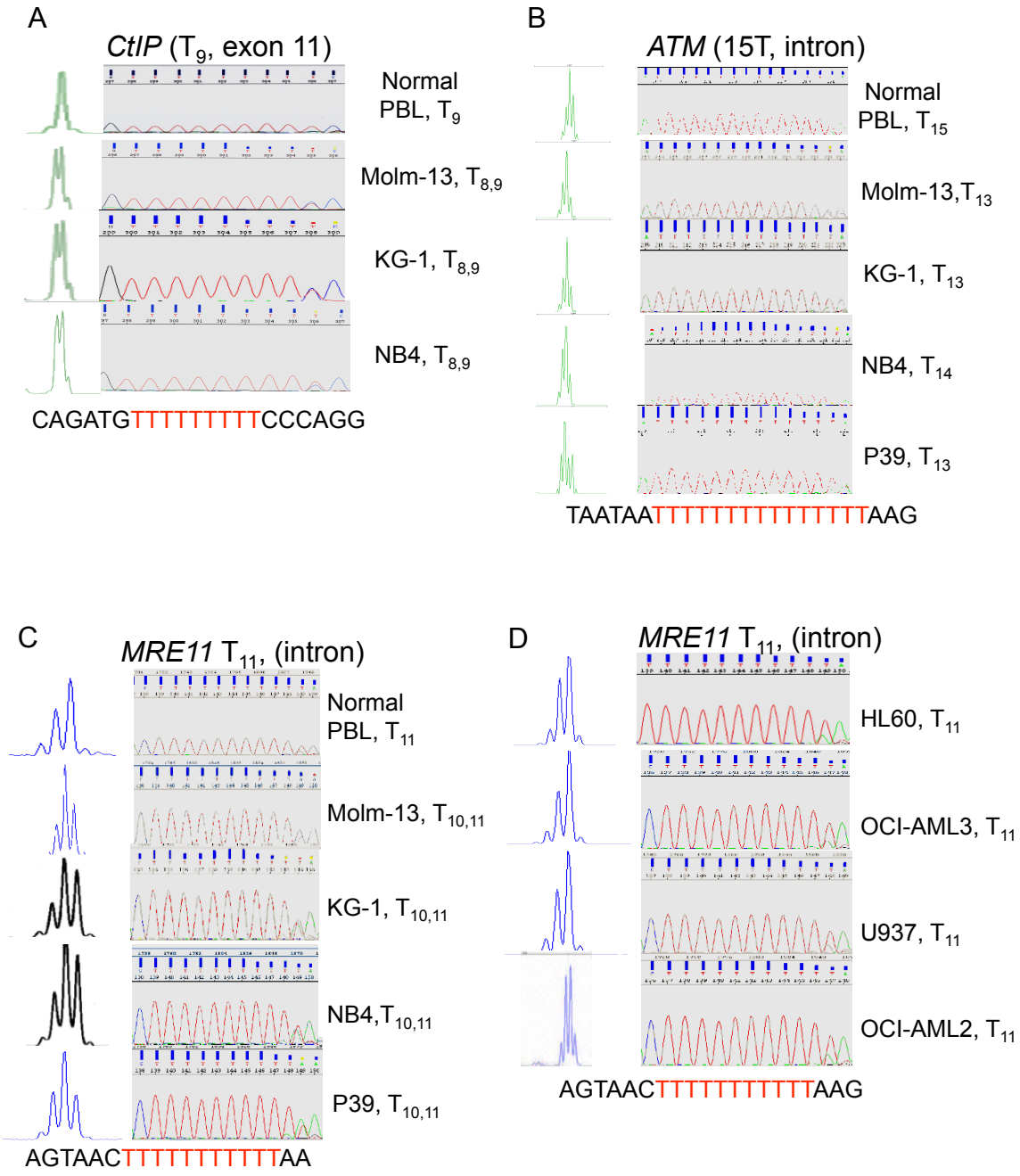
2. Plummer R, Jones C, Middleton M, Wilson R, Evans J, Olsen A, Curtin N, Boddy A, McHugh P, Newell D, *et al*. Phase 1 study of the poly(ADP-ribose) polymerase inhibitor, AG014699, in combination with temozolomide in patients with advanced solid tumors. *Clin. Can. Res*. 2008; 14:7917-7923.

Supplementary Figure S1



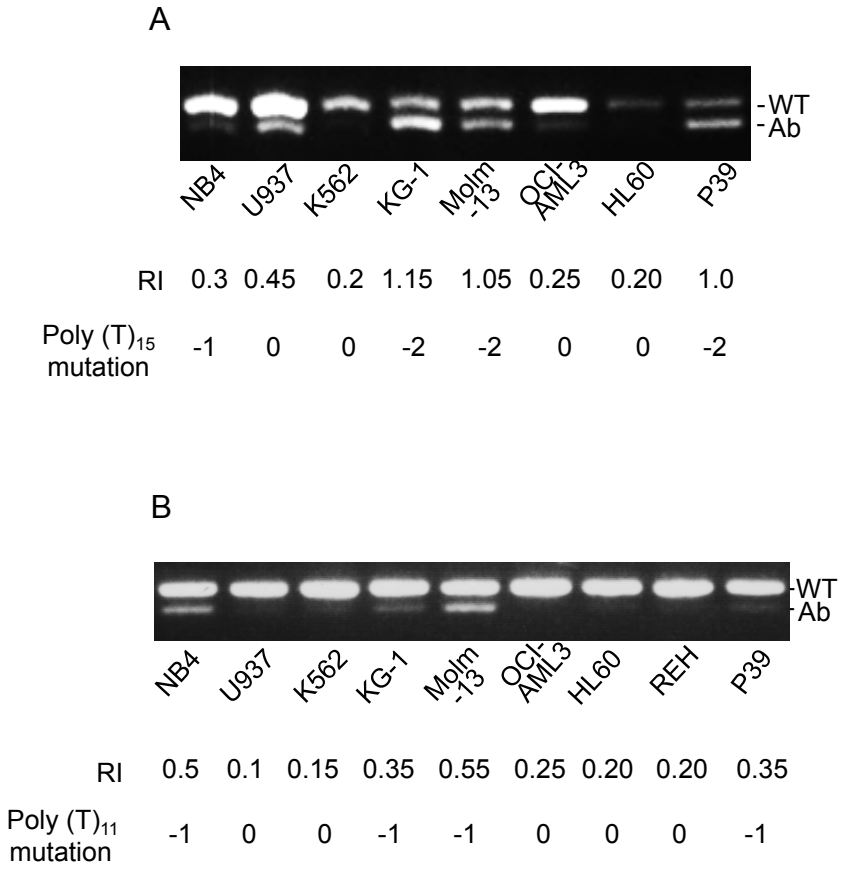

**Supplementary Figure S1. MSI profiling analysis in MDS/AML cell lines** (A-B) MSI loci profiles of MDS/AML cell line and normal PBL DNA using fluorescent fragment PCR for (A), NR21 and (B), BAT26 microsatellites. Arrows depict mean size of PCR product from normal PBL. Microsatellite sequence is shown under respective profile.

Supplementary Figure S2



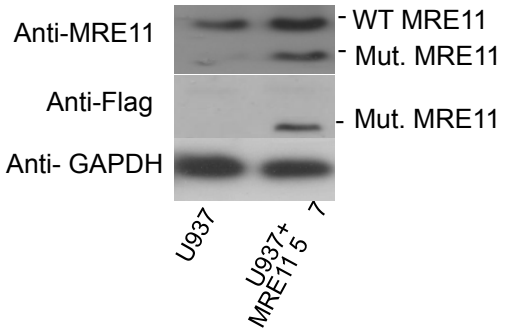

**Supplementary Figure S2 Fluorescent fragment PCR and sanger sequencing of DNA repair gene coding region microsatellites.** (A-D), DNA from MDS/AML cell lines and normal PBL were used in PCR reactions for (A), *CtIP*, 9 thymine microsatellite ($T_9$, exon 11), (B), *ATM*, 15 thymine microsatellite ($T_{15}$, intronic) and (C-D) *MRE11*, 11 thymine ($T_{11}$, intronic). Fluorescent fragment profile is shown in left panel, sanger sequence is shown in right panel. Microsatellite sequence is shown under respective profile.

Supplementary Figure S3



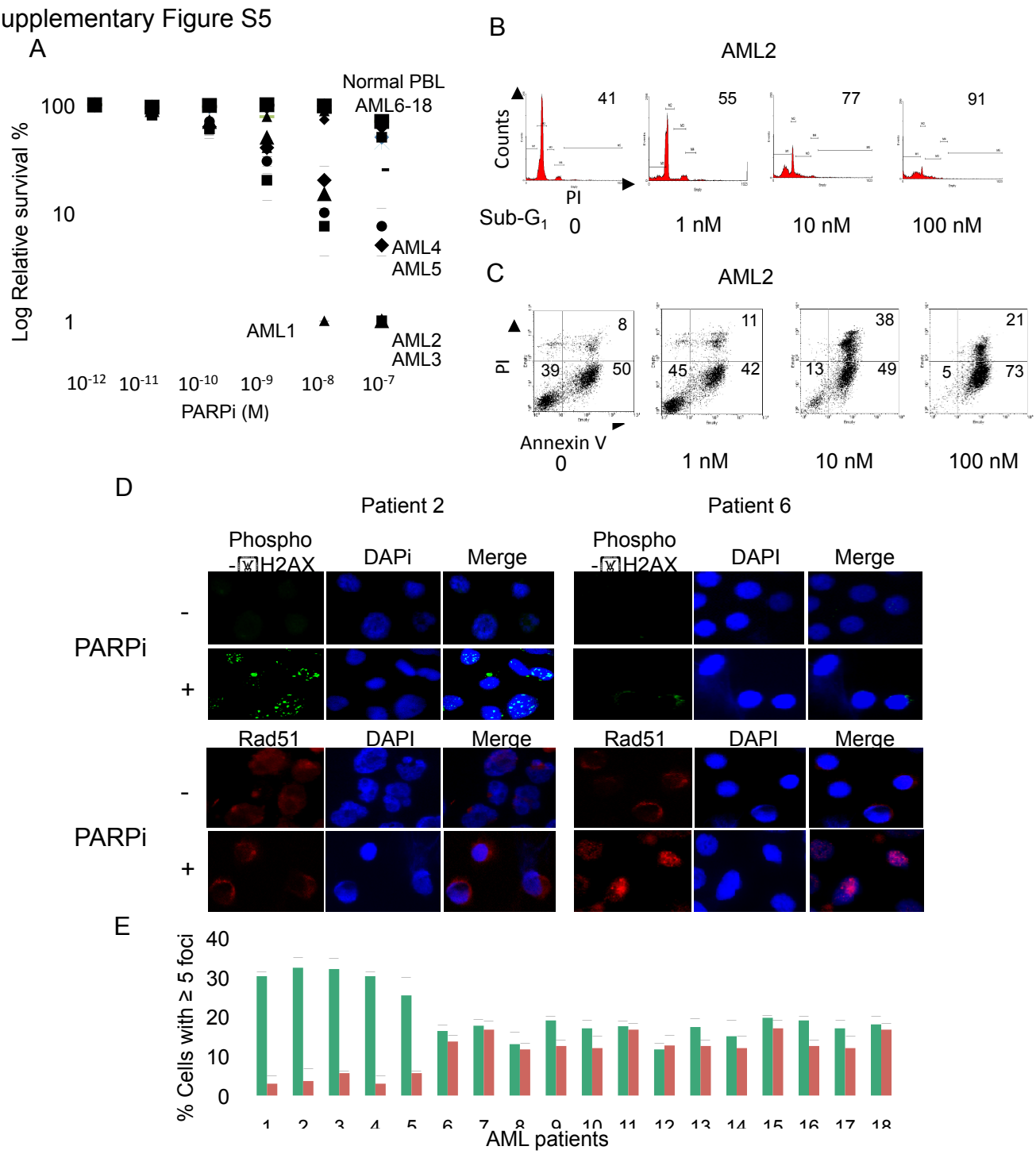

**Supplementary Figure S3. Aberrant gene transcripts of *ATM* and *MRE11* in MDS/AML cell lines**. PCR amplification for (A), exon 8 of *ATM* and (B) exon 5 for *MRE11* were performed on cDNA from MDS/AML cell lines. Ratio of intensities (RI) between wild-type (WT) and aberrant (Ab) transcript were determined by measuring the intensity of gel bands using Adobe Photoshop™.

Supplementary Figure S4



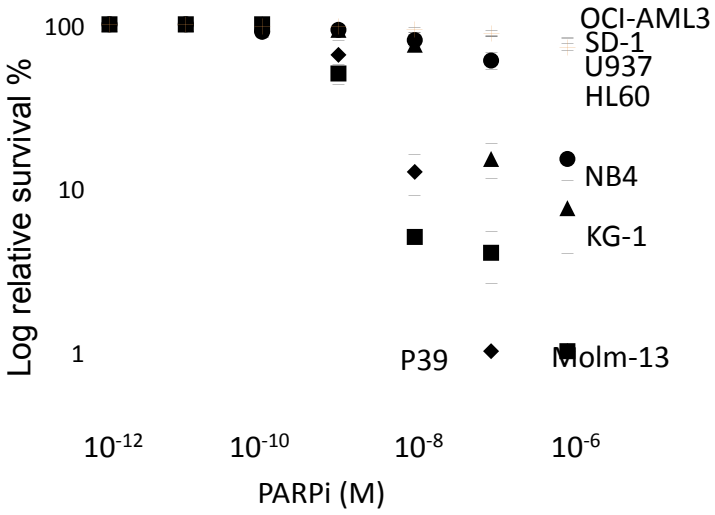

**Supplementary Figure S4** Mutant *MRE11* 5[illegible]7 in pIRESpURO3 was stably transfected into U937. *MRE11* 5[illegible]7 contains a C-terminal FLAG sequence and immunoblots were probed with anti-MRE11 and anti-FLAG.

Supplementary Figure S5



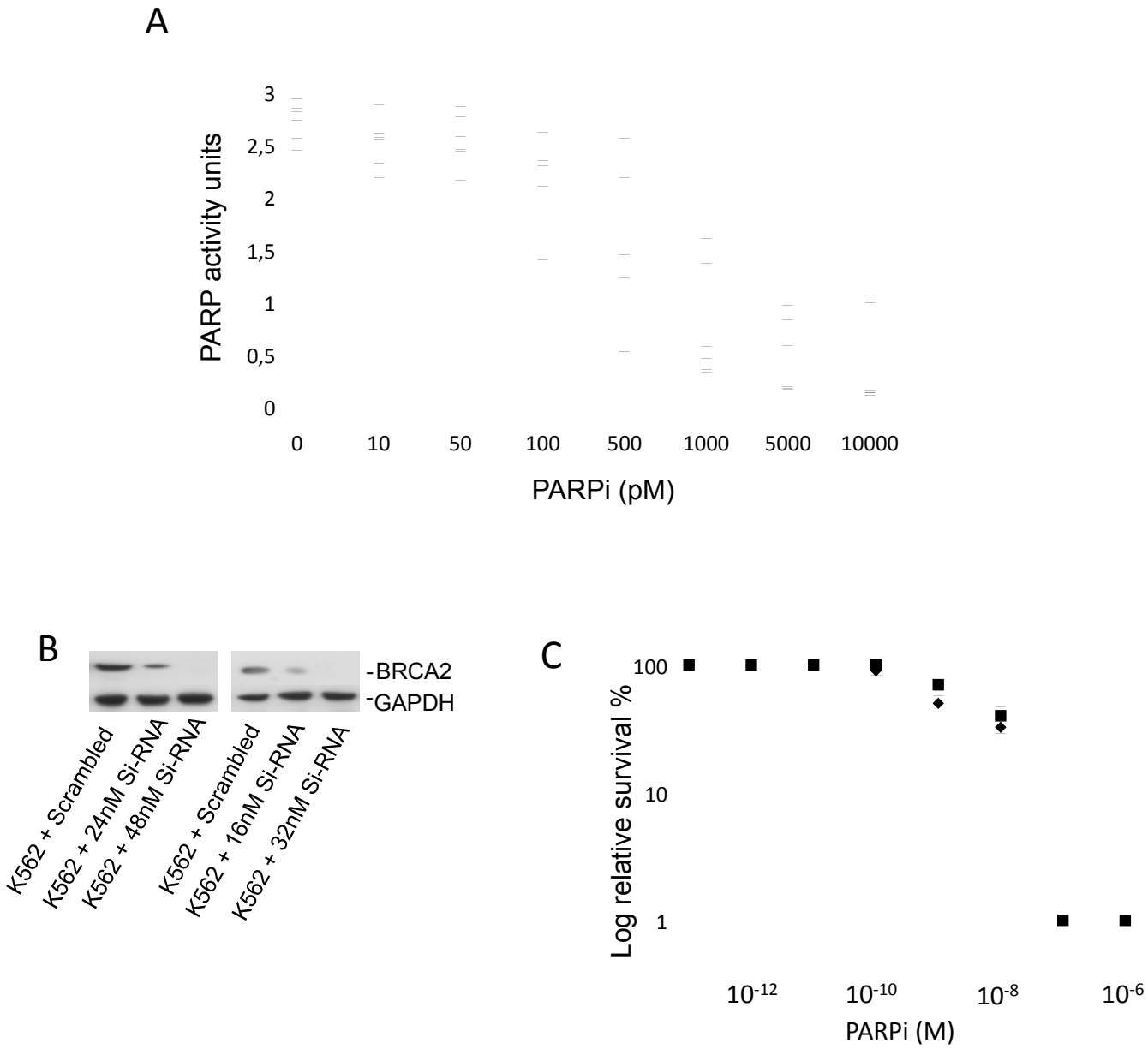

**Supplementary Figure S5 The effect of PARPi on primary AML cell survival**. (A). Viability analysis using trypan blue exclusion assays. Primary AML cells and normal peripheral blood lymphocytes (PBL) were cultured with increasing concentrations of PARPi continuously for 120 h. AML1 (open triangles), AML2 (solid squares), AML3 (solid triangles), AML4 (solid circles), AML5 (solid diamonds), AML6-18 and normal PBL (As indicated) (Error bars represent the means ± S.E.M. of three separate experiments. (B), Analysis by flow cytometry. Increasing PARPi concentrations were added to AML patient 2 cells for 120 h. The apoptotic index (sub-$G_1$ population as a fraction of the total population, is shown right inset). (C), Analysis by Annexin V on the cell surface. Increasing concentrations of PARPi were added to AML patient 2 cells for 120 h before being treated with annexin V-FITC (FL-1, X-axis) and propidium iodide (PI) (FL-2, Y-axis). The figures show the percentage of non-apoptotic (bottom left quadrant), early (bottom right quadrant) and late apoptotic cells. (top right quadrant). D,E, DSB DNA repair by immunohistochemistry of rad51 and phospho-γH2AX foci. (D), Representative immunostaining of nuclei from primary AML cells treated with 100 nM PARPi for 24 h. Cells were probed for phospho-γH2AX or rad51 foci and nuclei were stained with DAPI. E, Frequency of cells displaying phospho-γH2AX foci (%) (green bars) or rad51 foci (%) (red bars), by immunofluorescence following PARPi addition in (B) primary AML and (C) MDS/AML cell lines. 200 nuclei were counted per experiment. Error bars represent the means ± S.E.M. of three separate experiments.

Supplementary Figure S6



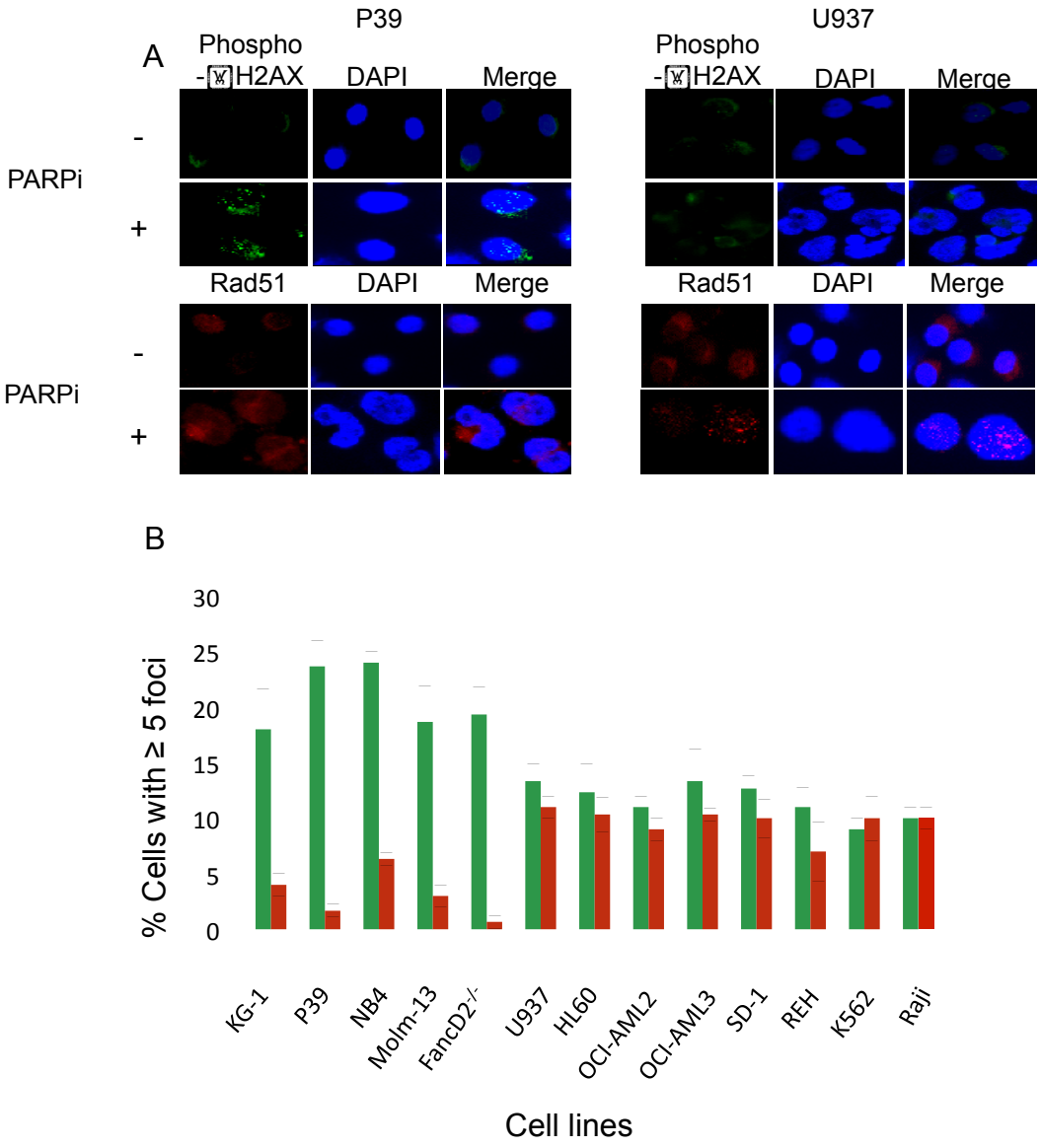

**Supplementary Figure S6**. **The effect of PARPi on MDS/AML cell line survival**. (A), Cell survival was assessed by soft agar clonogenic assay. Cells were exposed to variable concentrations of PARPi for 120 h before cloning in soft agar for a further 14 days. P39 (☒), Molm-13 (■), KG-1 (▲), NB4 (•), OCI-AML3 (X), SD-1 (+), U937 (o), HL60 (✳)

Supplementary Figure S7




**Supplementary Figure S7. PARPi abrogation of PARP activity**. A. Comparison of PARPi. PARP enzyme activity assays using increasing concentrations of BMN 673 (blue), KU-0058948 (red) and PJ34 (green) were conducted as per manufacturer's instructions using nuclear extract from AML patient 2 cells as a source of PARP enzyme. B, K562 cells were transfected with BRCA2 Si-RNA (Dharmacon, left panels) and (Santa Cruz, right panels) using nucleofection. C, BRCA2 Si-RNA transfected K562 were treated with PARPi for a further 24h before cloning in soft agar for a further 14 days. BRCA2 Si-RNA (Dharmacon) (▩), BRCA2 Si-RNA (Santa Cruz) (■).

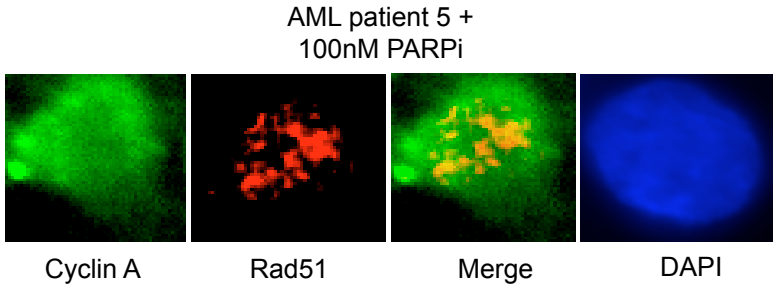
Supplementary Figure S8



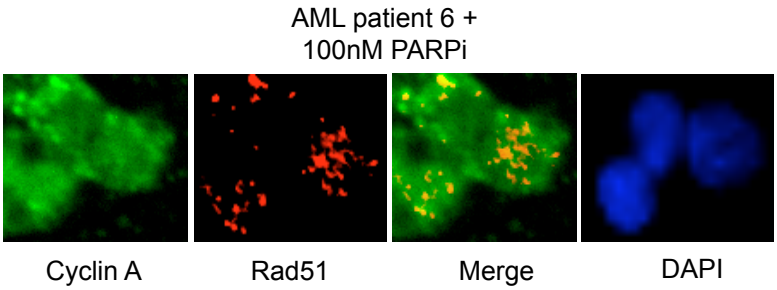

**Supplementary Figure S8 Immunostaining of nuclei from MDS/AML cell lines.** A, Cells were treated with 100 nM PARPi for 24 h in PARP sensitive P39 cells (left) and PARPi insensitive U937 (right). Representative foci from cells probed for phospho-γH2AX foci or rad51 foci and nuclei were stained with DAPI. B, Detection of frequency of cells displaying phospho-γH2AX foci (%) (green bars) or rad51 foci (%) (red bars), by immunofluorescence following PARPi addition. More than 200 nuclei were counted per experiment. Mean ±S.E.M were determined in three separate experiments.

Supplementary Figure S9

A




B

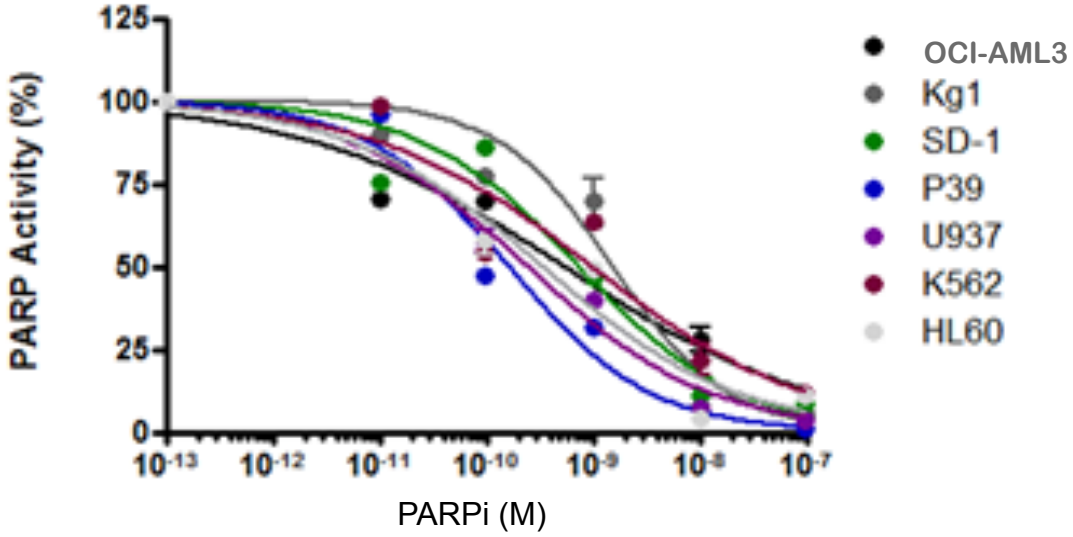



C

| AML Patient | Cyclin A % | Rad51 foci in cyclin A +ve cells% |
|---|---|---|
| 2 | 32±2 | 97±3 |
| 5 | 35±2 | 100±2 |
| 6 | 30±5 | 98±2 |

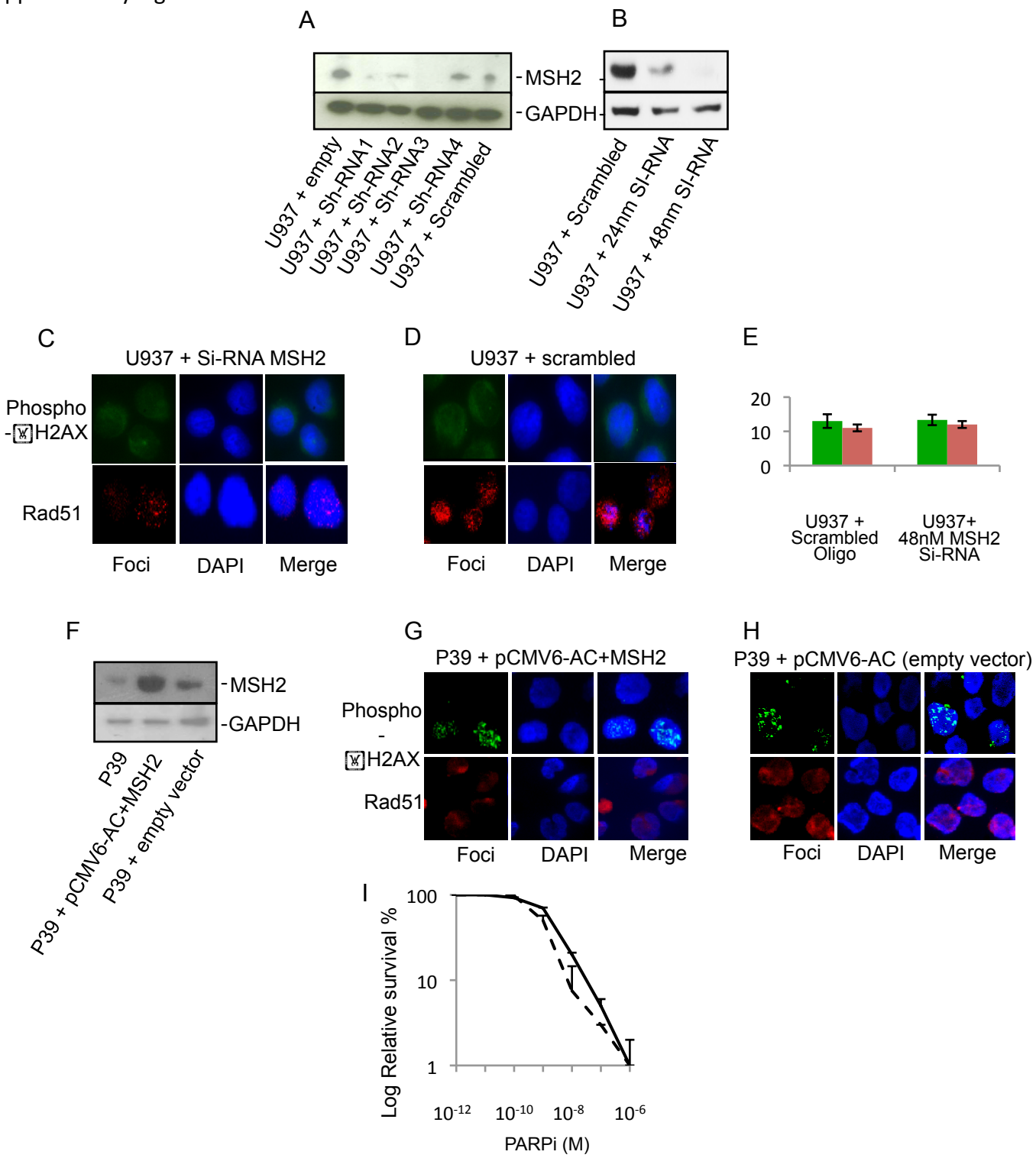
**Supplementary Figure S9**. Mutant MRE11 and mutant CtIP do not affect cell cycle distribution of rad51 foci after DSB damage. A, Log phase AML patient 5 and 6 cells were treated with 100 nM PARPi for 24 h and immunostained for cyclin A, rad51 and counterstained with DAPI. Representative images are shown. B, Frequency of cells displaying cyclin A(%) or rad51 foci (%) (red bars), by immunofluorescence following PARPi addition in AML patients cells (n=3).

Supplementary Figure S10




**Supplementary Figure S10. Dose response curves of intrinsic PARP activity in MDS/AML cell lines.** Dose response curves of intrinsic PARP activity in MDS/AML cell lines. Increasing PARPi concentration was added to cells prior to the determination of PAR accumulation. Cells were stimulated by exposing permeabilised cells to blunt-ended oligonucleotide in the presence of $NAD^+$.

Supplementary Figure S11




**Supplementary Figure S11. Modulation of MMR.** A,B Immunoblots were prepared from whole cell extracts of U937 cells transfected with A, SH-RNA vectors (SH-RNA 1-4) and B, Si-RNA to MSH2. Scrambled oligonucleotides acted as silencing controls for Sh-RNA and Si-RNA. Immunoblots were probed with anti-MSH2 and anti-GAPDH. C,D Representative immunostaining of nuclei from C, U937 + Si-RNA MSH2 and D, U937 + scrambled oligo control, pre-treated with 100nM PARPi for 24 h. E, Frequency of cells displaying phospho-γH2AX foci (%) (green bars) or rad51 foci (%) (red bars), by immunofluorescence following PARPi addition in MSH2 Si-RNA depleted cells and scrambled oligo. controls. 200 nuclei were counted per experiment. Error bars represent the means ± S.E.M. of three separate experiments. F-I, Over-expression of MSH2. F, pCMV6-AC + MSH2 sequence was stably transfected into P39 cells. Immunoblots were probed with anti-MSH2 and anti-GAPDH. G-I, Representative immunostaining of nuclei from G, P39 + pCMV6-AC+MSH2 (over-expressed MSH2) and H, P39 + pCMV6-AC (empty vector) pre-treated with 100nM PARPi for 24 h. I, P39 + pCMV6-AC+MSH2 (over-expressed MSH2, solid line), P39 + pCMV6-AC (empty vector, dashed line) PARPi was incubated for 120 h before plating on soft agar for 14 days.

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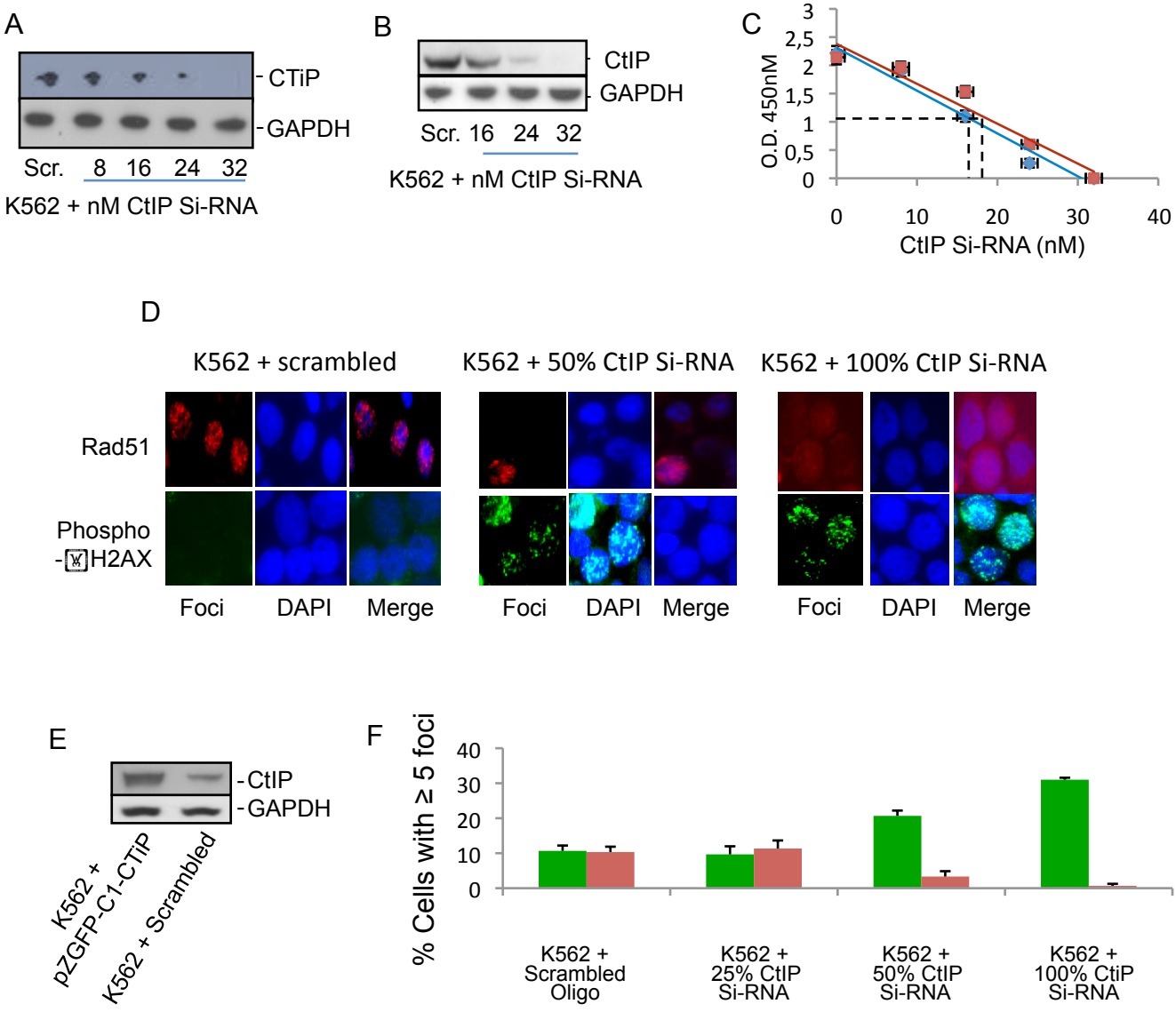
Supplementary Figure S12




**Supplementary Figure S12** A-B Increasing concentrations of Si-RNA (A, Dharmacon, B, Santa Cruz) to CtIP were transfected into K562 by nucleofection and immunoblots probed with anti-CTiP. Scrambled oligonucleotides acted a silencing control. C, ELISA standard curve prepared of increasing concentrations of Si-RNA (Dharmacon, blue diamonds), B, Santa Cruz, red squares) to CtIP transfected into K562 by nucleofection. Extracts were prepared and ELISA for CtIP expression was performed. Dotted line interpolates the concentration of si-RNA to give 50% of CTiP expression. D, Representative rad51 and phospho-γH2AX foci after treatment with 100 nM PARPi for 24 h in K562 + scrambled oligo (left panel), 50% (19nM) CtIP Si-RNA (Santa Cruz, Center panel), and K562 + 100% (32nM) CtIP Si-RNA (right panel) E, Over-expression of CtIP. K562 was transfected with the CtIP over-expressing plasmid, pZGFP-C1-CtIP or with a scrambled oligonucleotide control. F, Frequency of phospho-γH2AX foci positive cells (%) (green bars) and rad51 foci positive cells (%) (red bars) following 24 h PARPi addition. Error bars represent the means ± S.E.M. of three separate experiments.

Supplementary Table S1 Clinical and Cytogenetic information for the AML patient cohort. BM – Bone marrow, PB – Peripheral Blood.

| Patient | Sample | FAB | Cytogenetics |
|---|---|---|---|
| AML 1 | No Data | No Data | No data |
| AML 2 | BM | M2 (tAML) | t(6;10)(q27;q21)[5]/46,XY,del(1)(q25q32),add(4)(q35) |
| AML 3 | BM | M5 | Failed |
| AML 4 | PB | CML→AML M4 | Failed |
| AML 5 | BM | M1 | +4,t(6;9)(p23;q34),t(15;17)(q15;q11) |
| AML 6 | PB | MDS/AML M4 | Normal |
| AML 7 | PB | M2 | Normal |
| AML 8 | BM | M4 | Normal |
| AML 9 | BM | M5 | Normal |
| AML 10 | BM | M5 | +8 |
| AML 11 | BM | M5 | +4, +8, +21 |
| AML 12 | BM | MDS-AML M4 | -7 |
| AML 13 | BM | M6 | Normal |
| AML 14 | No Data | No Data | No data |
| AML 15 | No Data | No Data | No data |
| AML 16 | No Data | No Data | No data |
| AML 17 | No Data | No Data | No data |
| AML 18 | No Data | No Data | No data |

**Supplementary Table S2 Correlation of MSI and HR competency in MDS/AML cell lines**. Microsatellite loci were analyzed by fluorescent fragment PCR. Bi-allelic MSI panel deletions (≥ 3bp) are indicated as open circles (○). Closed circles (●) indicate no MSI (MSI panel PCR products < 3bp) or no deletions in DNA repair gene microsatellites. ○/● indicate the presence of mono-allelic MSI panel PCR products or mono-allelic DNA repair gene microsatellite deletions. For HR competency, HR dysfunction is indicated as crosses.

| Cell Line | MSI Panel | | | | | | DNA repair genes | | | | | | | | | | | | | | HR | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | NR21 | NR22 | NR24 | BAT25 | BAT26 | MONO27 | ATM | ATR | BRCA1 | BRCA2 (9) | BRCA2(22) | BLM | CHk1 | CtIP | DNA-PKcs | MRE11 | PTEN | PARP1 | TNK1 | RAD50 | | TGF-βII |
| FANCD2$^{-/-}$ | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | X | • |
| HL60 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| K562 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| KG-1 | ○/• | ○/• | • | ○ | ○/• | ○/• | ○/• | • | • | • | • | • | • | ○/• | • | ○/• | • | • | • | • | X | • |
| Molm-13 | ○ | ○/• | • | ○/• | ○/• | ○ | ○/• | • | • | • | • | • | • | ○/• | • | ○/• | • | • | • | • | X | • |
| NB4 | ○/• | ○/• | • | ○/• | ○/• | ○/• | ○/• | • | • | • | • | • | • | ○/• | • | ○/• | • | • | • | • | X | • |
| OCI-AML2 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| OCI-AML3 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| P39 | ○ | ○/• | • | ○ | ○/• | ○ | ○/• | • | • | • | • | • | • | ○/• | • | ○/• | • | • | • | • | X | • |
| Raji | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| REH | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| SD-1 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| U937+ shRNA-MSH2 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| U937+ control vector | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| P39+ pCMV6-AC+MSH2 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| P39+ pCMV6 (Empty Vector) | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |

**Supplementary Table S3. Correlation of MSI and HR competency in AML patients**. Microsatellite loci were analyzed by fluorescent fragment PCR. Bi-allelic MSI panel deletions (≥ 3bp) are indicated as open circles (○). Closed circles (●) indicate no MSI (MSI panel PCR products < 3bp) or no deletions in DNA repair gene microsatellites. ○/● indicate the presence of mono-allelic MSI panel PCR products or mono-allelic DNA repair gene microsatellite deletions. HR competency, HR defective is indicated by crosses. Therapy related AML (t-AML) patient is indicated by an asterisk (*).

| AML | MSI Panel | | | | | | DNA repair genes | | | | | | | | | | | | | | HR | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | NR21 | NR22 | NR24 | BAT25 | BAT26 | MONO27 | ATM | ATR | BRCA1 | BRCA2 (9) | BRCA2(22) | BLM | CHK1 | CtIP | DNA-PKcs | MRE11 | PTEN | PARP1 | TNK1 | RAD50 | | TGF-βII |
| 1 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | X | • |
| 2* | ○/• | • | ○/• | • | ○/• | ○/• | • | • | • | • | • | • | • | • | • | ○/• | • | • | • | • | X | • |
| 3 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | X | • |
| 4 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | X | • |
| 5 | ○/• | • | • | • | ○ | ○/• | • | • | • | • | • | • | • | ○/• | • | • | • | • | • | • | X | • |
| 6 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 7 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 8 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 9 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 10 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 11 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 12 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 13 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 14 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 15 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 16 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 17 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| 18 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |

**Supplementary Table S4 Intrinsic PARP activity of MDS/AML cell lines**. Cells were stimulated by exposing permeabilised cells to blunt-ended oligonucleotide in the presence of $NAD^+$.

| MDS/AML cell line | Basal unstimulated PAR (nmol) per $10^6$ cells | Basal stimulated PAR (nmol) per $10^6$ cells | PARPi Sensitivity |
|---|---|---|---|
| P39 | 1.3 | 39.2 | ++ |
| KG1 | 1.7 | 84.7 | + |
| SD-1 | 1.1 | 30.8 | - |
| OCI-AML3 | 1.6 | 57.3 | - |
| U937 | 1.2 | 58.8 | - |
| K562 | 1.6 | 43.2 | - |
| HL60 | 0.3 | 29.4 | - |

**Supplementary Table S5. Chromosomal locations and aberrations in 63 high risk MDS patient determined by SNP analysis**. For MSI, L=MSI-low, H=MSI-high and N=negative. For TP53, WT = wild type, Mut. = Mutated. For Type, LOH = copy neutral loss of heterozygosity, (LOH)/UPD, NA = No aberrations. Therapy related MDS (t-MDS) patients are indicated by an asterisk (*).

| MDS patient | MSI | TP53 | Type | Chromosome | Cytoband Start | Cytoband End | Size (bp) |
|---|---|---|---|---|---|---|---|
| **1** | L | WT | LOH | 11 | q12.3 | q25 | 72,246,167 |
| **2** | H | WT | LOH | 2 | p25.3 | p16.3 | 46,931,070 |
| | | | Loss | 5 | q23.1 | q32 | 28,599,727 |
| | | | Loss | 7 | p22.3 | q36.3 | 156,256,445 |
| **3** | L | WT | LOH | 11 | q13.1 | q25 | 67,782,871 |
| **4** | L | WT | LOH | 7 | q22.1 | q36.3 | 57,408,500 |
| **5** | H | Mut. | Loss | 1 | q24.2 | q24.2 | 3,326,516 |
| | | | Loss | 1 | q42.13 | q42.3 | 7,483,492 |
| | | | Loss | 4 | q21.23 | q35.2 | 105,967,537 |
| | | | Loss | 5 | q33.2 | q33.2 | 340,119 |
| | | | Loss | 5 | q31.3 | q31.3 | 445,640 |
| | | | Loss | 5 | q14.3 | q15 | 3,399,516 |
| | | | Loss | 5 | q23.2 | q31.2 | 12,587,265 |
| | | | Loss | 7 | p22.3 | q36.3 | 158,604,880 |
| | | | Loss | 12 | p11.22 | q12 | 12,065,388 |
| | | | Loss | 12 | p13.33 | p12.1 | 20,011,424 |
| | | | Loss | 12 | q21.1 | q24.33 | 61,384,780 |
| | | | Loss | 16 | p13.3 | q24.3 | 88,301,897 |
| | | | Loss | 17 | p13.3 | p11.2 | 19,127,603 |
| | | | Loss | 20 | q11.22 | q13.33 | 26,051,760 |
| | | | Loss | 21 | q11.2 | q21.2 | 9,398,158 |
| **6** | L | Mut | Loss | 7 | q11.23 | q36.3 | 81,592,379 |
| | | | Gain | 9 | p24.3 | p12 | 40,543,174 |
| | | | Loss | 9 | q13 | q34.3 | 70,071,368 |
| | | | Loss | 18 | q22.1 | q22.1 | 839,580 |
| | | | Gain | 18 | q21.1 | q21.1 | 853,313 |
| | | | Gain | 18 | q12.1 | q12.1 | 916,710 |
| | | | Gain | 18 | q12.3 | q12.3 | 1,082,691 |
| | | | Gain | 18 | q21.1 | q21.1 | 1,851,938 |
| | | | Loss | 18 | q22.3 | q23 | 3,641,787 |
| | | | Gain | 18 | q22.1 | q22.3 | 7,209,487 |
| | | | Gain | 18 | q21.2 | q22.1 | 14,562,004 |
| | | | Gain | 20 | q13.31 | q13.33 | 6,023,652 |
| | | | Gain | 20 | q13.2 | q13.33 | 8,459,277 |
| | | | Loss | 21 | q21.1 | q21.1 | 2,034,128 |
| | | | Loss | 21 | q21.1 | q21.3 | 5,063,530 |
| | | | Loss | 21 | q22.11 | q22.13 | 6,523,769 |
| | | | Gain | 21 | q22.13 | q22.3 | 9,862,454 |
| **7** | H | WT | Gain | 1 | q21.3 | q44 | 96,150,471 |
| | | | Loss | 6 | q14.1 | q14.1 | 1,662,513 |
| | | | Loss | 7 | q11.22 | q31.33 | 58,583,639 |
| | | | Gain | 9 | p24.3 | q12 | 69,231,244 |

Supplementary Table S5

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **8** | L | WT | LOH | 20 | q11.21 | q13.33 | 32,606,676 |
| | | | Loss | 21 | q22.12 | q22.12 | 952,246 |
| **9** | L | WT | LOH | 6 | p22.2 | p21.32 | 7,289,924 |
| | | | Loss | 7 | q22.1 | q36.3 | 59,221,010 |
| | | | Gain | 9 | p24.3 | p13.1 | 37,563,330 |
| **10** | L | WT | Gain | 3 | q23 | q29 | 55,618,436 |
| | | | Loss | 7 | p22.3 | p14.2 | 35,421,613 |
| | | | Loss | 18 | p11.32 | p11 | 14,859,205 |
| | | | Loss | 18 | q21 | q23 | 24,989,855 |
| | | | Gain | 18 | q11.1 | q21.2 | 34,300,911 |
| | | | LOH | 21 | q21.3 | q22.3 | |
| **11** | H | WT | LOH | 2 | p14 | p12 | 10,988,646 |
| | | | LOH | 4 | q31.22 | q31.3 | 7,196,190 |
| | | | LOH | 9 | p21.2 | p13.2 | 11,110,432 |
| | | | LOH | 19 | q12 | q13.2 | 7,684,988 |
| **12*** | L | WT | Loss | 7 | p22.3 | q36.3 | 158,409,722 |
| | | | LOH | 13 | q12.13 | q34 | 87,664,433 |
| **13*** | L | Mut. | Loss | 6 | p21.32 | p21.32 | 429,074 |
| | | | Loss | 6 | p21.1 | p21.1 | 1,345,937 |
| | | | Gain | 6 | p21.31 | p21.2 | 3,743,048 |
| | | | Loss | 6 | p23 | p22.1 | 11,577,909 |
| | | | Loss | 6 | p25.3 | p23 | 13,937,899 |
| | | | Loss | 7 | p14.1 | q36.3 | 118,980,258 |
| | | | Gain | 18 | q21.1 | q21.2 | 1,445,313 |
| | | | Loss | 18 | q21.1 | q21.1 | 1,760,639 |
| | | | Loss | 18 | q21.31 | q21.32 | 2,568,307 |
| | | | Loss | 18 | q22.1 | q23 | 15,448,142 |
| | | | Gain | 18 | q11.1 | q21.1 | 26,380,056 |
| | | | Loss | 21 | q22.11 | q22.12 | 1,032,303 |
| **14** | N | WT | NA | NA | NA | NA | NA |
| **15** | N | WT | NA | NA | NA | NA | NA |
| **16** | N | WT | NA | NA | NA | NA | NA |
| **17** | N | WT | NA | NA | NA | NA | NA |
| **18** | N | WT | loss | X | p11.4 | p11.4 | 2,410,192 |
| | | | loss | 3 | q26.2 | q26.2 | 403,464 |
| **19** | N | Mut. | Loss | 5 | q31.2 | q35.3 | 42,795,999 |
| | | | Gain | 17 | q24.3 | q24.3 | 589,218 |
| | | | Gain | 17 | q23.2 | q23.3 | 665,042 |
| | | | Gain | 17 | q24.2 | q24.2 | 1,561,077 |
| | | | Loss | 17 | q24.3 | q25.1 | 1,714,932 |
| | | | Gain | 17 | q25.2 | q25.2 | 1,874,682 |
| | | | Loss | 17 | q24.2 | q24.3 | 2,186,420 |
| | | | Loss | 17 | p13.3 | p13.1 | 10,228,035 |
| | | | Loss | 17 | p13.1 | p11.2 | 11,089,216 |
| **20** | N | WT | Loss | 11 | p15.5 | p15.4 | 1,101,866 |
| **21** | N | WT | NA | NA | NA | NA | NA |

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **22** | N | WT | Gain | 1 | p32.3 | p32.3 | 832,764 |
| | | | Gain | 1 | p35.1 | p34.1 | 12,694,360 |
| | | | Loss | 1 | p36.33 | p35.2 | 31,041,095 |
| | | | Loss | 5 | p15.33 | p11 | 42,345,754 |
| | | | Loss | 5 | q14.3 | q35.3 | 97,686,987 |
| | | | Gain | 7 | q21.2 | q21.3 | 4,909,738 |
| | | | Loss | 7 | q22.1 | q33 | 37,306,046 |
| | | | Gain | 17 | p13.1 | p12 | 4,762,509 |
| | | | Loss | 17 | q21.33 | q22 | 5,384,700 |
| | | | Gain | 17 | p11.2 | q11.1 | 5,742,949 |
| | | | Gain | 17 | q22 | q23.2 | 5,978,707 |
| | | | Loss | 17 | q11.2 | q12 | 8,740,685 |
| | | | Loss | 17 | p13.3 | p13.1 | 8,979,444 |
| | | | Loss | 17 | q24.3 | q25.3 | 10,227,513 |
| | | | Gain | 21 | q22.13 | q22.3 | 9,186,979 |
| **23** | N | WT | Loss | 5 | q31.2 | q31.2 | 990,832 |
| | | | Loss | 5 | q13.3 | q13.3 | 1,126,845 |
| | | | Gain | 11 | q13.4 | q25 | 61,270,945 |
| | | | Loss | 17 | q11.2 | q11.2 | 2,457,176 |
| **24** | N | Mut. | Loss | 5 | q11.1 | q35.3 | 131,161,016 |
| | | | Loss | 6 | p21.31 | p21.31 | 1,477,361 |
| | | | Gain | 6 | p21.31 | p21.2 | 2,160,378 |
| | | | Loss | 6 | p21.2 | p21.1 | 2,714,594 |
| | | | Gain | 6 | p21.1 | p12.3 | 6,042,249 |
| | | | Gain | 6 | p22.2 | p21.31 | 9,685,287 |
| | | | Loss | 6 | p25.3 | p22.2 | 25,238,463 |
| | | | Loss | 7 | p12.1 | p12.1 | 270,872 |
| | | | Loss | 7 | q22.1 | q22.1 | 1,739,336 |
| | | | Gain | 7 | p15.2 | p14.3 | 7,908,955 |
| | | | Loss | 7 | p14.3 | p12.1 | 18,664,719 |
| | | | Loss | 7 | p22.3 | p15.2 | 26,258,663 |
| | | | Gain | 7 | p12.1 | q22.1 | 47,000,330 |
| | | | Gain | 15 | q22.31 | q26.3 | 38,010,049 |
| | | | Loss | 15 | q11.2 | q22.31 | 39,979,291 |
| | | | Gain | 19 | q12 | q13.43 | 31,028,595 |
| **25** | N | WT | Loss | 7 | p22.3 | q36.3 | 158,805,161 |
| | | | Loss | 12 | p13.2 | p13.1 | 1,621,380 |
| **26** | N | WT | Loss | 7 | p22.3 | q36.3 | 158,812,470 |
| | | | LOH | 17 | q21.32 | q25.3 | 36,053,322 |
| **27** | N | WT | NA | NA | NA | NA | NA |
| **28** | N | Mut. | Loss | 5 | p15.33 | p14.3 | 22,354,035 |
| | | | Loss | 5 | q11.2 | q33.3 | 108,844,776 |
| | | | Loss | 17 | p13.3 | p11.2 | 16,201,282 |
| | | | Gain | 19 | q12 | q13.43 | 30,772,620 |
| **29** | N | Mut. | Loss | 1 | q21.3 | q24.2 | 6,358,346 |
| | | | Gain | 1 | p36.33 | q21.3 | 150,237,257 |

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **29** | N | Mut. | Loss | 3 | p21.1 | q13.13 | 58,719,043 |
| | | | Loss | 5 | q11.2 | q35.3 | 126,174,982 |
| | | | Gain | 7 | q21.13 | q21.13 | 1,475,518 |
| | | | Gain | 7 | q21.3 | q22.1 | 2,266,285 |
| | | | Gain | 7 | q21.11 | q21.11 | 3,429,101 |
| | | | Loss | 7 | q22.1 | q36.1 | 51,383,635 |
| | | | Loss | 11 | p12 | p12 | 3,765,499 |
| | | | Loss | 18 | p11.32 | p11.21 | 12,593,432 |
| | | | Loss | 18 | q12.1 | q23 | 52,578,994 |
| | | | Gain | 19 | p13.3 | p13.11 | 11,377,279 |
| | | | Loss | 21 | q22.3 | q22.3 | 2,140,795 |
| **30** | N | WT | NA | NA | NA | NA | NA |
| **31** | N | WT | Loss | 7 | p22.3 | q36.3 | 158,604,880 |
| **32** | N | WT | NA | NA | NA | NA | NA |
| **33** | N | Mut. | Loss | 3 | q26.2 | q26.2 | 474,136 |
| | | | Loss | 3 | q21.3 | q21.3 | 1,211,973 |
| | | | Loss | 7 | q21.3 | q36.3 | 68,868,000 |
| | | | Loss | 7 | p22.3 | p11.2 | 58,761,999 |
| **34** | N | WT | NA | NA | NA | NA | NA |
| **35** | N | WT | Gain | 8 | p23.3 | q24.3 | 146,268,948 |
| | | | Loss | 21 | q22.12 | q22.12 | 1,202,318 |
| **36** | N | Mut. | Loss | 3 | p25.2 | p24.3 | 6,713,571 |
| | | | Gain | 3 | q25.2 | q29 | 43,928,347 |
| | | | Loss | 5 | q11.1 | q12.1 | 13,048,970 |
| | | | Loss | 5 | q12.2 | q35.3 | 117,332,202 |
| | | | Loss | 7 | p11.2 | q36.3 | 103,799,684 |
| | | | Gain | 11 | q23.1 | q25 | 37,876,450 |
| | | | Loss | 13 | q12.3 | q21.33 | 37,613,578 |
| | | | Loss | 18 | p11.31 | p11.21 | 7,449,195 |
| | | | Loss | 18 | q22.2 | q23 | 11,592,865 |
| | | | Loss | 20 | p13 | p13 | 1,317,978 |
| | | | Loss | 20 | q11.23 | q13.32 | 21,084,879 |
| **37** | N | WT | Gain | X | p22.33 | q13.1 | 70,951,090 |
| | | | Loss | X | q13.1 | q28 | 82,862,904 |
| **38** | N | WT | Loss | 7 | p22.3 | q36.3 | 156,690,906 |
| **39** | N | WT | NA | NA | NA | NA | NA |
| **40** | N | WT | Loss | 7 | q21.11 | q36.3 | 71,620,655 |
| **41** | N | Mut. | Loss | 2 | p25.1 | p23.3 | 15,116,825 |
| | | | Loss | 5 | q15 | q34 | 67,728,653 |
| | | | Loss | 7 | q11.21 | q36.3 | 92,942,222 |
| | | | Gain | 8 | p23.3 | q24.3 | 145,619,410 |
| | | | Gain | 12 | p12.3 | p12.3 | 761,314 |
| | | | Loss | 12 | p13.33 | p13.33 | 2,442,057 |
| | | | Gain | 12 | p13.33 | p13.31 | 2,941,334 |
| | | | Gain | 12 | p12.2 | p12.1 | 5,550,278 |
| | | | Loss | 12 | p13.31 | p12.3 | 12,957,571 |

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **41*** | N | Mut. | Gain | 13 | q13.3 | q14.11 | 22,256,520 |
| | | | Loss | 16 | q21 | q24.3 | 30,151,806 |
| | | | Loss | 17 | p13.3 | p13.1 | 6,890,047 |
| | | | LOH | 17 | p13.1 | p11.2 | 9,938,138 |
| | | | Loss | 20 | q11.22 | q12 | 8,340,967 |
| **42** | N | WT | Gain | X | p22.33 | q13.2 | 72,105,045 |
| | | | Loss | X | q13.2 | q28 | 82,618,613 |
| **43** | N | WT | NA | NA | NA | NA | NA |
| **44** | N | WT | NA | NA | NA | NA | NA |
| **45*** | N | Mut. | LOH | 1 | q32.1 | q44 | 44,251,250 |
| | | | Loss | 2 | p23.3 | p23.3 | 894,368 |
| | | | Loss | 5 | q13.2 | q13.3 | 988,421 |
| | | | Loss | 5 | q13.3 | q35.3 | 105,364,002 |
| | | | Gain | 6 | p25.3 | q27 | 170,013,200 |
| | | | Loss | 7 | q11.22 | q36.3 | 88,629,175 |
| | | | Gain | 8 | p23.3 | q24.3 | 145,358,662 |
| | | | Loss | 11 | p15.5 | p15.4 | 2,194,893 |
| | | | Gain | 11 | p15.4 | q25 | 11,048,675 |
| | | | LOH | 11 | q13.3 | q24.1 | 53,306,391 |
| | | | Gain | 12 | p13.33 | p13.32 | 8,365,844 |
| | | | Loss | 12 | p13.31 | p11.21 | 21,491,742 |
| | | | Gain | 13 | q11 | q34 | 96,047,764 |
| | | | Loss | 16 | q12.1 | q21 | 7,042,932 |
| | | | Loss | 16 | q23.1 | q24.3 | 14,261,151 |
| | | | LOH | 17 | p13.3 | p13.1 | 8,586,041 |
| **46** | N | Mut. | Loss | 5 | q12.3 | q13.1 | 2,502,865 |
| | | | Loss | 5 | q14.1 | q35.3 | 99,891,001 |
| | | | LOH | 6 | q16.1 | q21 | 10,513,792 |
| | | | Loss | 7 | q11.23 | q36.3 | 83,878,779 |
| | | | Gain | 11 | q21 | q25 | 39,784,438 |
| | | | Loss | 12 | p13.32 | p12.3 | 12,373,525 |
| | | | LOH | 17 | p13.3 | p11.2 | 20,861,790 |
| | | | Loss | 18 | q21.2 | q23 | 29,282,490 |
| | | | Loss | 18 | p11.31 | q21.2 | 43,624,224 |
| **47** | N | WT | NA | NA | NA | NA | NA |
| **48** | N | Mut. | LOH | 1 | p33 | p32.1 | 11,398,167 |
| | | | Gain | 1 | p32.1 | p13.3 | 49,134,561 |
| | | | Gain | 1 | p36.33 | p32.3 | 52,408,141 |
| | | | Loss | 3 | q13.33 | q21.3 | 5,915,046 |
| | | | Loss | 3 | p24.3 | p24.1 | 5,959,345 |
| | | | Loss | 3 | p22.2 | p21.32 | 89,081,713 |
| | | | Loss | 5 | q13.2 | q14.1 | 6,968,612 |
| | | | Loss | 5 | q11.2 | q12.1 | 7,276,891 |
| | | | Loss | 5 | q23.3 | q34 | 33,246,379 |
| | | | Gain | 5 | p15.33 | q11.2 | 50,836,922 |
| | | | Loss | 7 | p14.2 | p14.1 | 4,470,952 |

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **48** | N | Mut. | Gain | 8 | p23.2 | q24.3 | 144,708,552 |
| | | | Gain | 9 | q32 | q34.3 | 21,626,846 |
| | | | Gain | 9 | p24.3 | p13.2 | 36,866,488 |
| | | | Gain | 11 | p15.4 | q25 | 134,449,983 |
| | | | Gain | 17 | p13.3 | p13.2 | 4,345,750 |
| | | | Loss | 17 | q11.2 | q12 | 4,997,615 |
| | | | Loss | 17 | p13.2 | p12 | 7,554,771 |
| | | | Gain | 22 | q11.1 | q13.33 | 34,678,319 |
| **49** | N | WT | Gain | 3 | q23 | q29 | 55,618,436 |
| | | | Loss | 7 | p22.3 | p14.2 | 35,421,613 |
| | | | Loss | 18 | p11.32 | p11 | 14,859,205 |
| | | | Loss | 18 | q21 | q23 | 24,989,855 |
| | | | Gain | 18 | q11.1 | q21.2 | 34,300,911 |
| | | | LOH | 21 | q21.3 | q22.3 | |
| **50** | N | WT | Loss | 7 | p22.3 | q36.3 | 158,805,161 |
| **51** | N | WT | Loss | 7 | p22.3 | q36.3 | 158,752,262 |
| **52** | N | WT | NA | NA | NA | NA | NA |
| **53** | N | WT | NA | NA | NA | NA | NA |
| **54** | N | WT | NA | NA | NA | NA | NA |
| **55** | N | WT | Loss | 2 | p24.1 | p23.3 | 3,297,060 |
| | | | Loss | 7 | p22.3 | p11.2 | 55,934,904 |
| | | | Loss | 7 | q21.13 | q36.3 | 67,965,029 |
| | | | Loss | 11 | q22.3 | q22.3 | 4,516,506 |
| | | | Loss | 11 | q14.1 | q14.1 | 5,744,116 |
| | | | Loss | 11 | q14.3 | q22.3 | 11,631,889 |
| | | | Loss | 12 | q12 | q12 | 4,921,459 |
| | | | Loss | 12 | q21.32 | q23.1 | 10,976,489 |
| | | | Loss | 12 | p13.2 | p11.1 | 23,704,288 |
| **56** | N | WT | Loss | 7 | p22.3 | q36.3 | 157,920,856 |
| **57** | N | WT | NA | NA | NA | NA | NA |
| **58** | N | Mut. | Gain | 3 | q23 | q29 | 58,434,963 |
| | | | Loss | 5 | q11.2 | q33.3 | 98,798,227 |
| | | | Loss | 7 | q22.1 | q36.3 | 58,934,837 |
| | | | Gain | 8 | p23.3 | q24.3 | 145,677,905 |
| | | | Loss | 20 | q11.21 | q13.2 | 19,615,525 |
| **59*** | N | Mut. | Loss | 3 | q13.13 | q21.1 | 14,861,617 |
| | | | Loss | 5 | q15 | q35.3 | 83,791,337 |
| | | | Loss | 7 | p22.3 | q36.3 | 158,733,375 |
| | | | Loss | 11 | p15.4 | p15.4 | 295,125 |
| | | | Loss | 12 | q13.13 | q13.13 | 1,463,962 |
| | | | Loss | 12 | p13.31 | p12.1 | 15,395,354 |
| | | | Loss | 14 | q24.2 | q24.3 | 2,256,796 |
| | | | Loss | 18 | q12.1 | q23 | 50,284,979 |
| | | | Loss | 21 | q11.2 | q21.1 | 5,178,668 |
| **60** | N | WT | Gain | 8 | p23.3 | q24.3 | 146,138,089 |
| | | | Gain | 21 | p11.2 | q22.3 | 37,162,644 |

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **61** | N | WT | Loss | 17 | p13.3 | p11.2 | 18,722,403 |
| | | | Gain | 17 | p11.2 | q25.3 | 59,621,574 |
| **62** | N | Mut. | Gain | 4 | q22.1 | q22.1 | 843,051 |
| | | | Gain | 20 | q13.32 | q13.33 | 5,927,727 |
| | | | Loss | 20 | p13 | p11.1 | 25,693,546 |
| | | | Loss | 20 | q11.21 | q13.32 | 25,984,652 |
| **63** | N | WT | Loss | 7 | q22.1 | q36.1 | 44,986,591 |