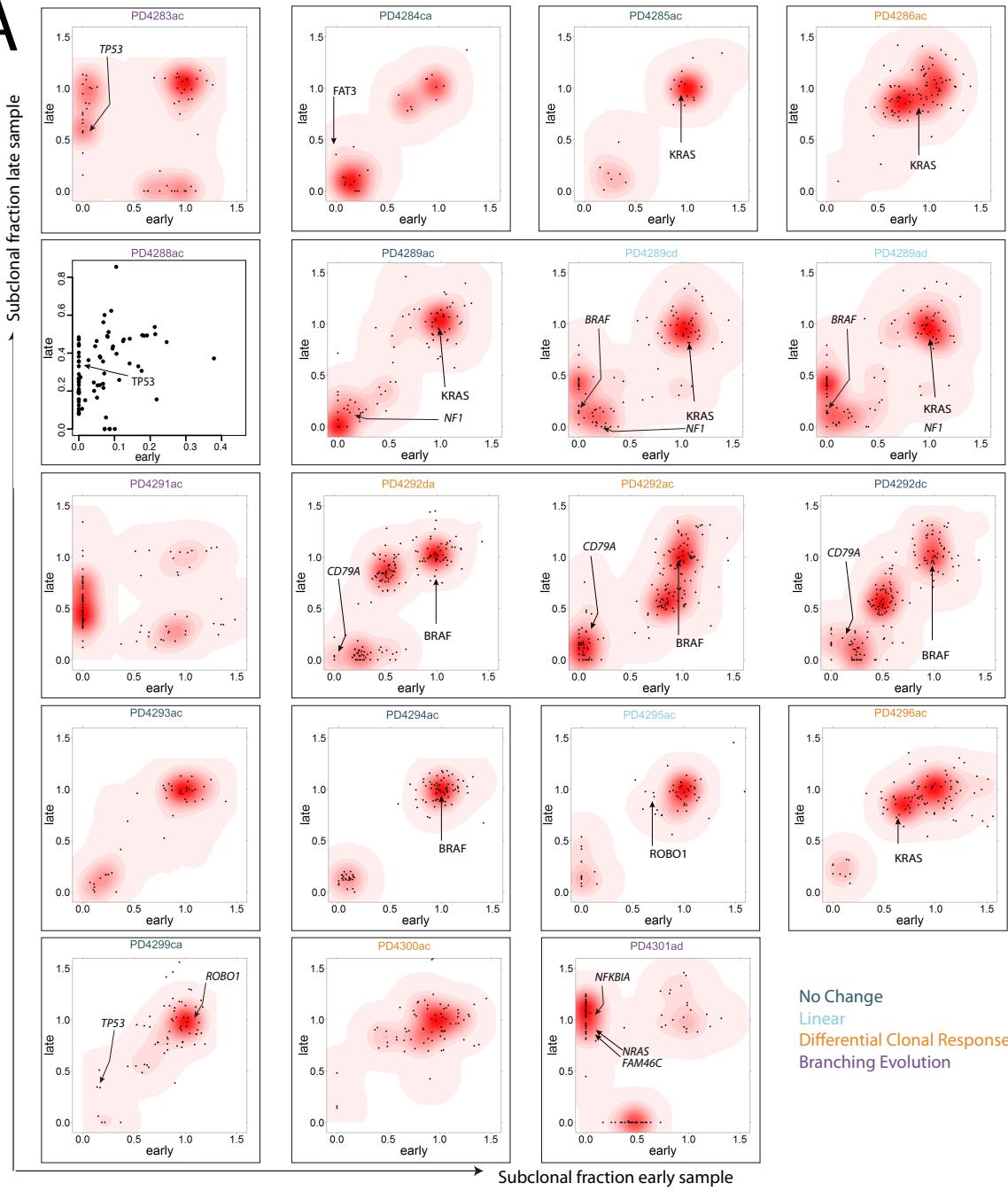


Supplementary Figure S1. Analysis of subclonal copy number changes and variants.

A): two copy number plots showing subclonal copy number changes (arrowheads), whose intensity is higher than clonal deletions (arrows) but lower than diploid chromosomes (asterisks). In each plot, purple=total copy number, blue=copy number of the minor allele.

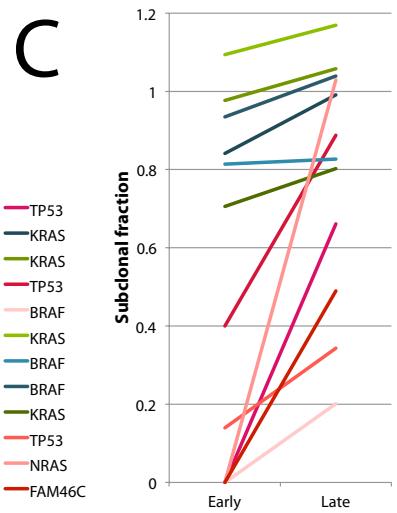
B): Statistical modeling by a Bayesian Dirichlet process of the distribution of clonal and subclonal mutations for all patients for which only 1 sample was available. For each plot, the fraction of tumor cells is represented on the X axis, and the probability density on the Y axis. The histogram of mutations is shown in grey, with the fitted distribution as a dark purple line. Also shown are the 95% posterior confidence intervals for the fitted distribution (pale blue area).

A

No Change
Linear
Differential Clonal Response
Branching Evolution

B

Karyotypic alterations				Genomic evolution by 2D Dirichlet Process		
Sample	Sample_type -(1p)	+ (1q)	Del(13)	Early vs Late	Late Vs Later	Early vs Late
PD4283a	Early	NO	NO	Subclonal		Branching
PD4283a	Late	YES	NO	NO		NO
PD4284c	Early	YES	NO	YES	YES	Branching
PD4284a	Late	YES	NO	YES	YES	No Change
PD4285a	Early	NO	NO	NO	NO	No Change
PD4285a	Late	NO	NO	NO	NO	No Change
PD4286a	Early	NO	NO	NO	NO	Dif. Clonal Response
PD4286c	Late	NO	NO	NO	NO	Dif. Clonal Response
PD4288a	Early	NO	NO	NO	YES	Branching
PD4288c	Late	NO	YES	YES	YES	Branching
PD4289a	Early	NO	NO	YES	NO	No Change
PD4289c	Late	NO	YES	NO		Linear
PD4289d	Later	NO	NO	Subclonal	NO	Linear
PD4291a	Early	NO	YES	NO	NO	Branching
PD4291c	Late	NO	YES	NO		Branching
PD4292d	Early	CN LOH	YES	NO	NO	Dif. Clonal Response
PD4292a	Late	CN LOH	YES	NO	NO	Dif. Clonal Response
PD4292c	Later	CN LOH	YES	NO	NO	Dif. Clonal Response
PD4293a	Early	NO	NO	YES	YES	No Change
PD4293c	Late	NO	NO	YES	YES	No Change
PD4294a	Early	NO	YES	YES	NO	No Change
PD4294c	Late	NO	YES	YES	NO	No Change
PD4295a	Early	NO	NO	NO	NO	Linear
PD4295c	Late	NO	NO	Subclonal	NO	Linear
PD4296a	Early	NO	YES	NO	YES	Dif. Clonal Response
PD4296c	Late	NO	YES	NO	YES	Dif. Clonal Response
PD4299c	Early	YES	NO	NO	NO	No Change
PD4299a	Late	YES	NO	NO	NO	No Change
PD4300a	Early	NO	YES	YES	NO	Dif. Clonal Response
PD4300c	Late	NO	YES	YES	NO	Dif. Clonal Response
PD4301a	Early	NO	YES	Subclonal	NO	Branching
PD4301d	Late	NO	YES	NO	NO	Branching

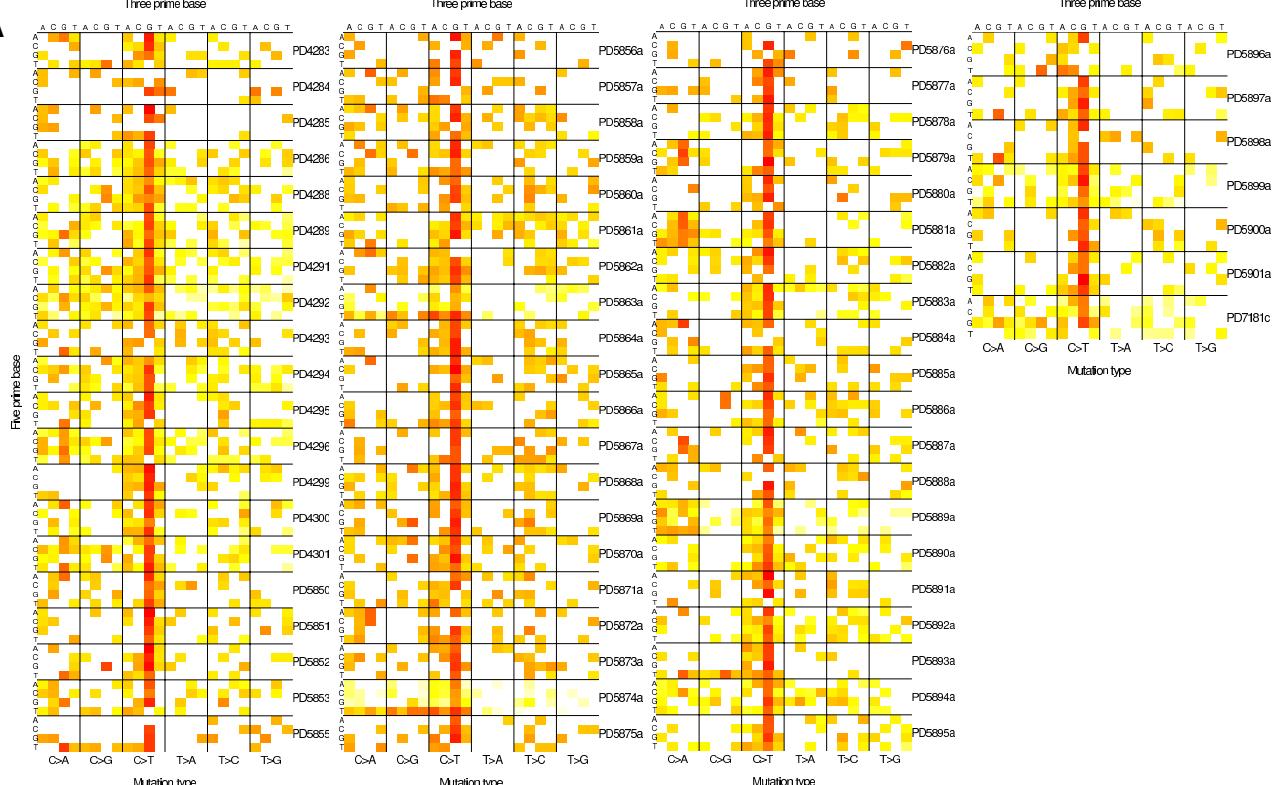
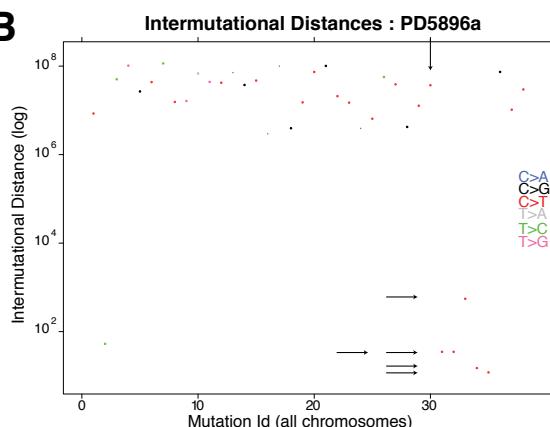
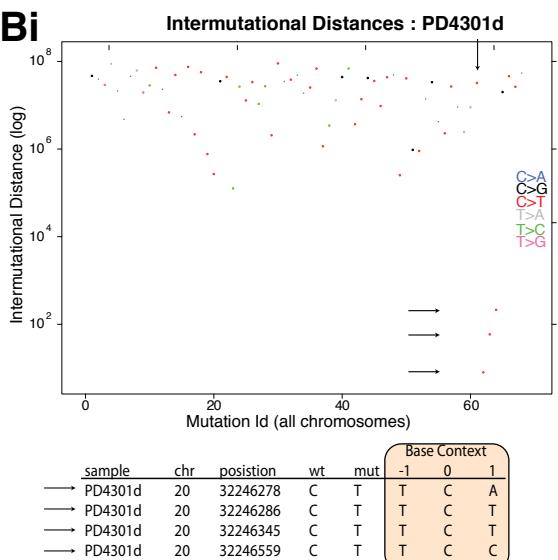


Supplementary Figure S2. Genomic evolution in 15 patients with serial samples

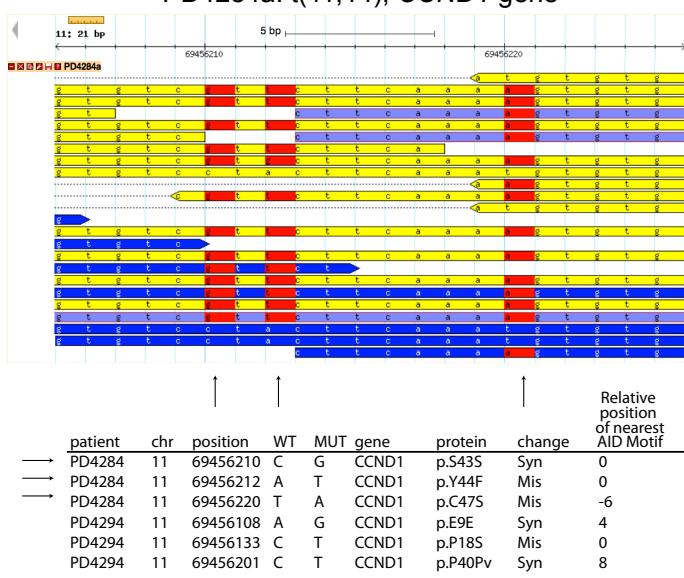
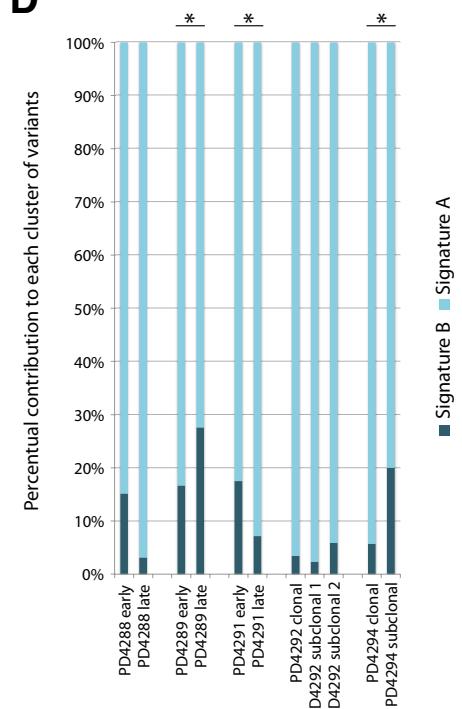
A) 2D density plots showing the clustering of the fraction of tumor cells carrying each mutation (black dots) at each time point; x=early sample, y=late sample; increasing intensity of red indicates the location of a higher posterior probability of a cluster. Each plot is titled with the concatenation of patient ID, X axis sample and Y axis sample, and the title is color-coded based on the type of evolution shown. For patients with 3 serial samples, 3 two-way comparisons have been made (PD4289 and PD42492). Note that for sample PD4288 ASCAT failed in estimating the normal cell contamination and the allele-specific copy number of the mutation; therefore, the Dirichlet process was not available and only the raw allelic fraction of each variant is plotted.

B) Table showing, for each of the 32 serial samples, the notable karyotypic features and the kind of genomic evolution of the tumor over time. Changes in karyotype over time in the same patient are highlighted in yellow. Note that karyotypic changes are only observed in patients showing linear or branching evolution.

C) Subclonal fraction of 12 putative driver mutations over time. 6 of them show an increase in their clonal fraction at the “late” time-point, consistent with the expected positive selection for the subclones harboring them (different shades of red).

A**B****Bi****C**

PD4284a. t(11;14), CCND1 gene

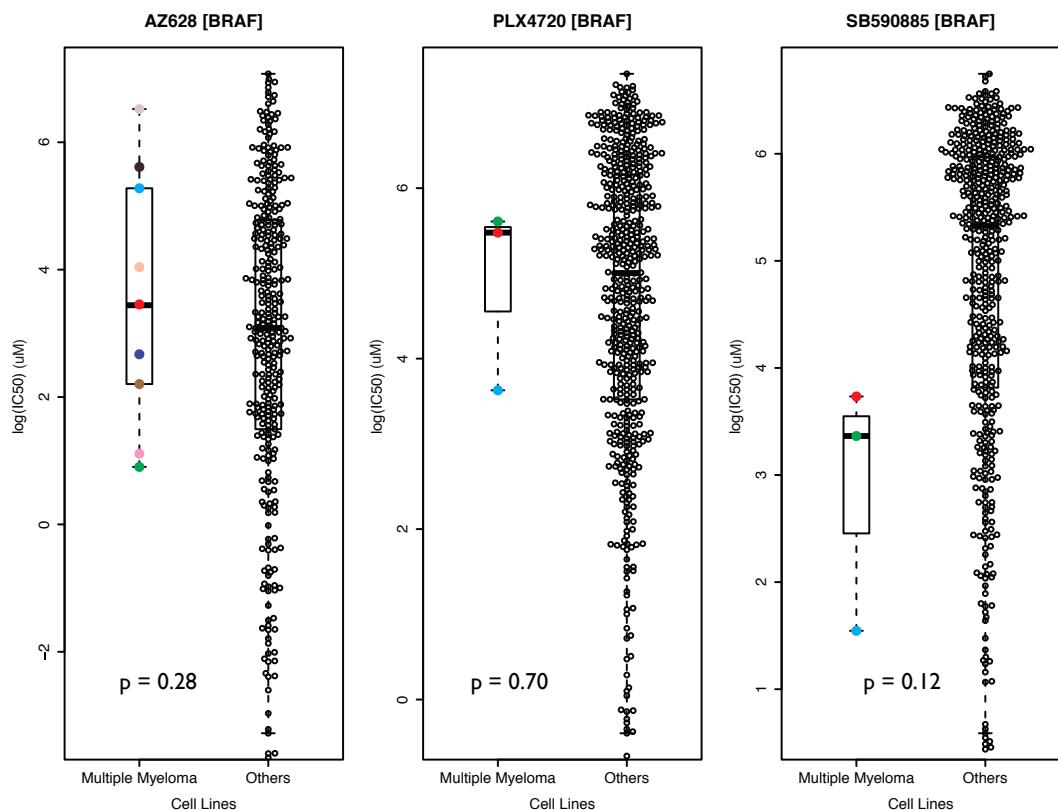
**D**

Supplementary Figure S3. Nucleotide change spectra.

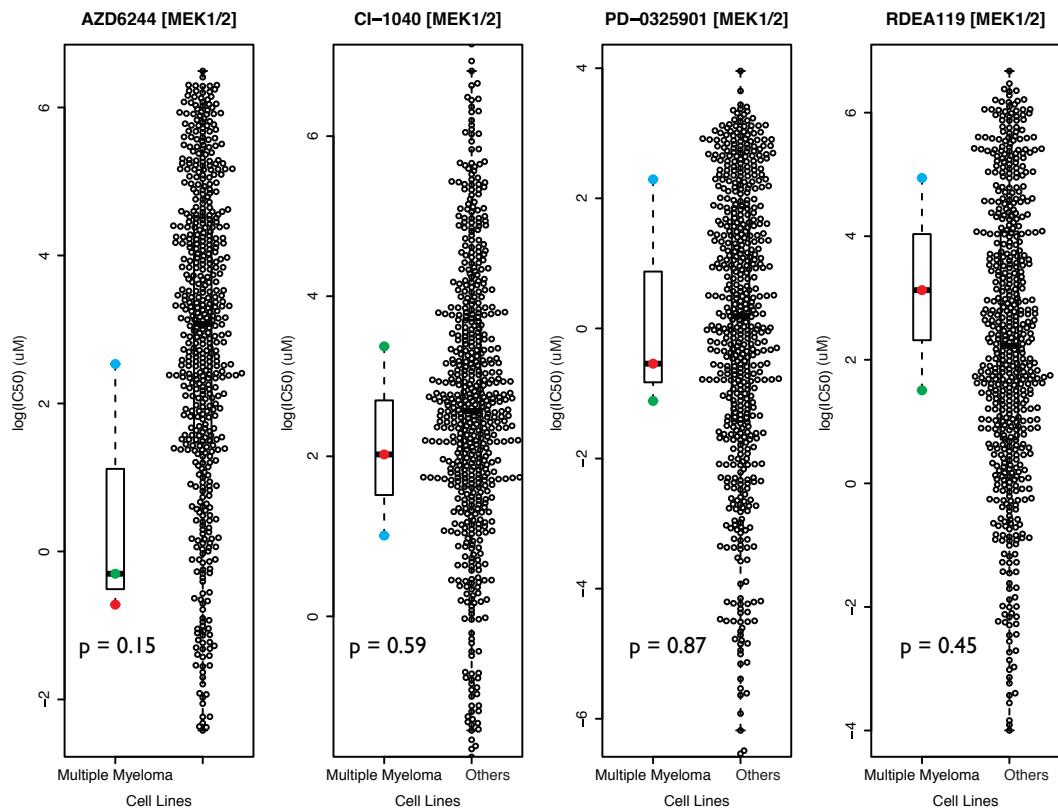
- A) Genomic heatmap built from counts of each mutation-type at each mutation context and corrected for the frequency of each trinucleotide in the reference genome. Log-transformed values of these ratios have been plotted in the heatmap. The 5' base to each mutated base is shown on the vertical axis and 3' base on the horizontal axis. The scale of colors varies from white (nucleotide change not observed in that context) to red (highest prevalence of the nucleotide change). Note in PD5863a and PD5874a the prevalence of C changes at TpCpX context (Signature B).
- B) Rainfall plot of PD5896a and PD4301d. Mutations are ordered on the X axis from the first variant on the short arm of chromosome 1 to the last variant on the long arm of chromosome X and are colored according to mutation-type. The distance between each mutation and the one before (the intermutation distance) is plotted on the vertical axis on a log scale. Most mutations have an intermutation distance of between 10^5 bp and 10^8 bp. Mutations in a region of hypermutation present as a cluster of lower intermutation distances, sharing the same nucleotide change (arrows) and context (as reported in the table).
- C) GBrowse image of a microcluster of variants in *CCND1* exon 1 in a patient with t(11;14), likely result of ongoing somatic hypermutation promoted by the AID protein. The position, nucleotide and protein change of *CCND1* mutation clusters in this patient (arrows) and in an additional case are reported in the table. Syn=synonymous, Mis=missense. AID recognition motif is defined as WRCY or RGYW.
- D) In samples from 5 patients, we compared the percentage contribution of the two mutational processes identified by NMF to the variants present in early sample vs late sample, or in the main clone vs subclones for samples showing no change over time (PD4294 and PD4292). A stacked bar chart shows that the contribution from

Signature B changes significantly in the samples marked with an asterisk (*) (Chi square test). Dark blue bars=Signature B, light blue bars=Signature A.

BRAF inhibitors



MEK1/2 inhibitors

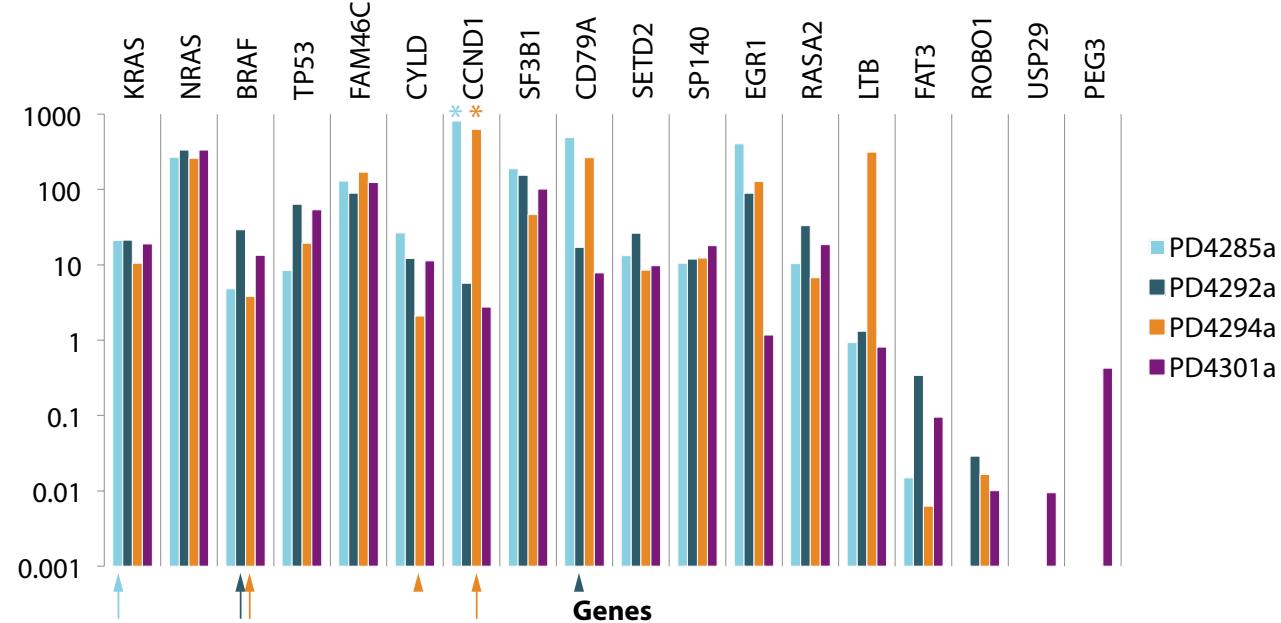


Cell Lines	BRAF	CDKN2C	KDM6A	KRAS	NRAS	PIK3CA	PTEN	TP53
IM-9					p.Q61K			
KMS-12-PE		Deleted	Deleted					p.R337L
SK-MM-2		Deleted	Deleted					p.K132N
U-266	p.K601N							p.A161T
RPMI-8226		Deleted		p.G12A				p.E285K
ARH-77								p.R273H
LP-1			p.Q541*					p.E286K
OPM-2		Deleted					Deleted	p.R175H
L-363			Deleted		p.Q61H	p.E545K		p.S261T

Supplementary Figure S4. Sensitivity of a panel of cell lines for selected BRAF and MEK inhibitors.

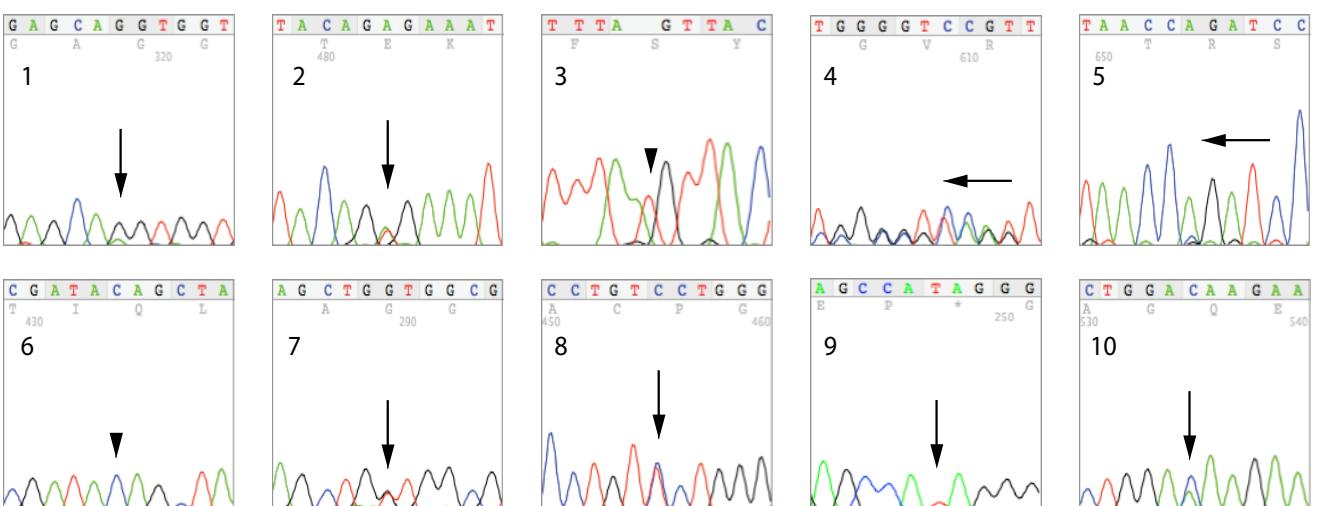
Scatter plots of cell lines half-maximal inhibitory concentration (IC50) for BRAF and MEK1/2 inhibitors as resulting from the large scale screen described in³⁴. IC50 values are on log scale and multiple myeloma cell lines are compared to those in the rest of screened panel. Each circle represents the IC50 of a cell line, horizontal bars represents geometric means and the boxes heights indicate standard deviation. Comparison between the two populations of IC50s in each plot has been performed through Welch's t-test and resulting p-values are reported. Each myeloma cell line is color-coded, and its relevant genotype is summarized at the bottom.

A



B

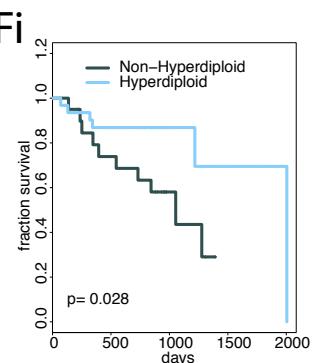
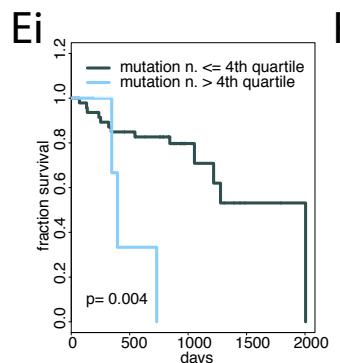
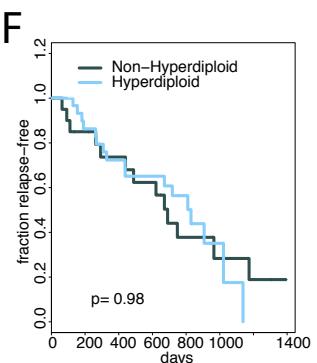
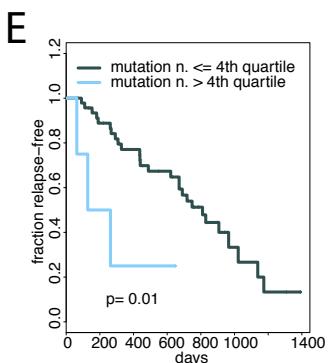
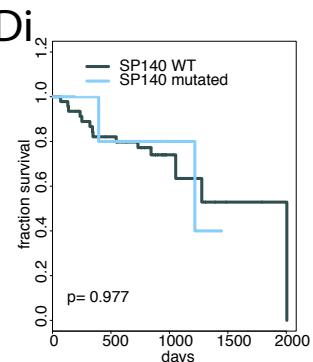
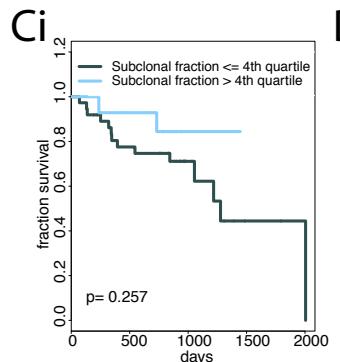
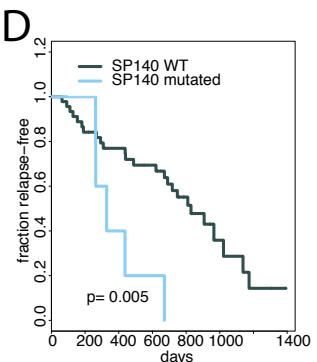
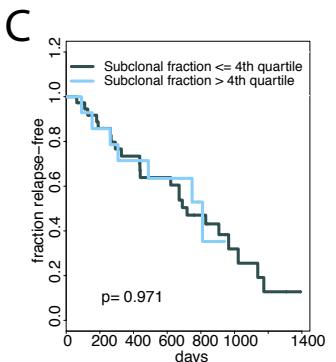
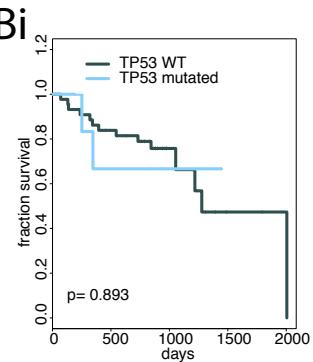
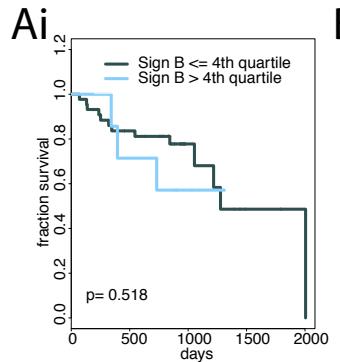
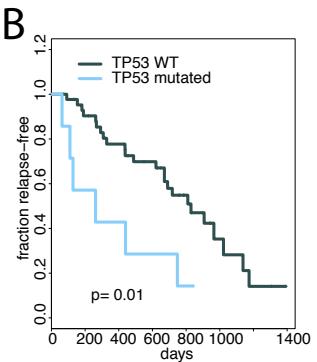
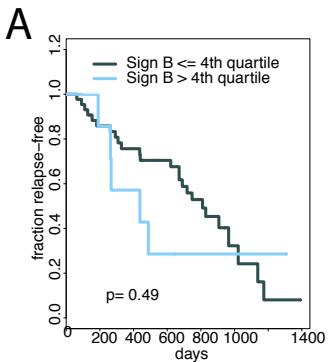
TRACE	SAMPLE	CHR	MIN POS	MAX POS	WT base	MUT base	TYPE	LENGTH	CHANGE	GENE	PROT	EXPRESSED
1	PD5851	1	115258748	115258748	C	T	S			NRAS	p.G12S	YES
2	PD5871	7	140453136	140453136	A	T	S			BRAF	p.V600E	YES
3	PD5872	13	73337716	73337716	A	T	S			DIS3	p.M667K	NO
4	PD5888	1	118166021	118166022	I			1	T	FAM46C	p.E178fs*1	YES
5	PD5888	3	141277738	141277738	D			1	C	RASA2	p.S233fs*11	YES
6	PD5888	12	25398255	25398255	G	T	S			KRAS	p.Q22K	NO
7	PD5890	12	25398284	25398284	C	A	S			KRAS	p.G12V	YES
8	PD5890	17	7577106	7577106	G	A	S			TP53	p.P278S	YES
9	PD5895	19	57325405	57325405	C	A	S			PEG3	p.E1469*	YES
10	PD5897	1	115256530	115256530	G	T	S			NRAS	p.Q61K	YES



Supplementary Figure S5. Expression of candidate genes

A) In 4 patients for which RNA-seq data was available, raw numbers of fragments per kilobase of exon per million fragments mapped (FKPM, Y axis) are plotted in logarithmic scale for 18 of the genes in the study. As an internal control of the quantitative value of the experiment, note CCND1 overexpression in two samples characterized by t(11;14) translocation (asterisks). Furthermore, mutated RNA transcripts were found for the genes mutated by whole exome sequencing (arrows), with the exception of two truncating mutations for which no mutated transcripts were identified (arrowheads), but rather only decreased overall expression.

B) For 7 additional patients, RT-PCR followed by capillary sequencing was performed on RNA to check for expression of 10 gene mutations described in the study. Traces are labeled following the numeration in column 1 of the table. Arrows highlight the mutation. Arrowheads point at the position where the mutation was expected, and show that the wild type sequence only is expressed. For indels, horizontal arrows indicate the direction of sequencing and the expected overlap of peaks.



Supplementary Figure S6. Survival Curves

Kaplan-Meier survival curves generated to compare relapse-free survival (A-F) and overall survival (Ai-Fi) of 51 patients based on the presence (light blue) or absence (dark blue) of: increased contribution from signature B (A-Ai), increased representation of subclonal variants (C-Ci), increased overall number of variants (E-Ei), TP53 mutations (B-Bi), SP140 mutations (D-Di), hyperdiploid karyotype (F-Fi). P-values are generated by a Longrank Significance Test. Note that quartiles were calculated based on values from the restricted cohort of 51 patients sampled at diagnosis.

SUPPLEMENTARY TABLE S1. PATIENT INFORMATION

Patient ID	Age at diagnosis	Karyotype or FISH	SNP6 data available	Disease status at 1st sample	Maximum disease response between 1st and 2nd sample		Disease status at 2nd sample	Evolution between 1st and 2nd sample	Days between 2nd and 3rd sample	Maximum disease response between 2nd and 3rd sample	Disease status at 3rd sample	Evolution between 2nd and 3rd sample
					Days between diagnosis and 1st sample	Days between 1st and 2nd sample						
PD4283	72	YES	Late sample only	Relapse	Yes	1781	402	Partial Remission	Relapse	branching		
PD4284	64	YES	Early sample only	Relapse	Yes	1565	618	Complete Remission	Relapse	no change		
PD4285	60	YES		Relapse	Yes	211	392	No Response	Progressive disease	no change		
PD4286	49	YES		Relapse	Yes	2436	77	No Response	Progressive disease	differential clonal response		
PD4288	57	YES		Relapse	Yes	1067	610	Very Good Partial Remission	Progressive disease	branching		
PD4289	55	YES	Late sample only	Relapse	Yes	1079	179	Very Good Partial Remission	Persistent disease	no change		
PD4291	46	YES	Late sample only	Relapse	Yes	1136	175	No Response	Persistent disease	branching		
PD4292	56	YES	NO	Relapse	Yes	2985	174	Partial Remission	Persistent disease	differential clonal response	299	Partial Remission
PD4293	67	YES		Relapse	Yes	1241	529	Complete Remission	Relapse	no change	184	Partial Remission
PD4294	53	YES		Relapse	Yes	1217	563	Very Good Partial Remission	Progressive disease	no change		
PD4295	61	YES	Late sample only	Relapse	Yes	98	452	Partial Remission	Persistent disease	linear		
PD4296	59	YES	Late sample only	Relapse	Yes	2117	157	No Response	Progressive disease	differential clonal response		
PD4299	56	YES	YES	Relapse	Yes	2317	180	Partial Remission	Persistent disease	no change		
PD4300	71	YES	Late sample only	Pre-Treatment	Yes	357	238	No Response	Progressive disease	differential clonal response		
PD4301	50	YES	NO	Relapse	Yes	1172	552	No Response	Progressive disease	branching		
PD7181	59	YES	NO	Relapse	No	1427						
PD5850	50	YES	NO	Pre-Treatment	No	0						
PD5851	66	YES	NO	Pre-Treatment	No	0						
PD5852	55	YES	NO	Pre-Treatment	No	0						
PD5853	57	YES	NO	Pre-Treatment	No	0						
PD5855	57	YES	NO	Pre-Treatment	No	0						
PD5856	85	YES	NO	Pre-Treatment	No	0						
PD5857	58	YES	NO	Pre-Treatment	No	0						
PD5858	82	YES	NO	Pre-Treatment	No	0						
PD5859	63	YES	NO	Pre-Treatment	No	0						
PD5860	52	YES	NO	Pre-Treatment	No	0						
PD5861	69	YES	NO	Pre-Treatment	No	0						
PD5862	75	YES	NO	Pre-Treatment	No	0						
PD5863	62	YES	NO	Pre-Treatment	No	0						
PD5864	79	YES	NO	Pre-Treatment	No	0						
PD5865	54	YES	NO	Pre-Treatment	No	0						
PD5866	74	YES	NO	Pre-Treatment	No	0						
PD5867	47	YES	NO	Pre-Treatment	No	0						
PD5868	64	YES	NO	Pre-Treatment	No	0						
PD5869	74	YES	NO	Pre-Treatment	No	0						
PD5870	64	YES	NO	Pre-Treatment	No	0						
PD5871	69	YES	NO	Pre-Treatment	No	0						
PD5872	49	YES	NO	Pre-Treatment	No	0						
PD5873	68	YES	NO	Pre-Treatment	No	0						
PD5874	54	YES	NO	Pre-Treatment	No	0						
PD5875	65	YES	NO	Pre-Treatment	No	0						
PD5876	73	YES	NO	Pre-Treatment	No	0						
PD5877	64	YES	NO	Pre-Treatment	No	0						
PD5878	72	YES	NO	Pre-Treatment	No	0						
PD5879	65	YES	NO	Pre-Treatment	No	0						
PD5880	61	YES	NO	Pre-Treatment	No	0						
PD5881	40	YES	NO	Pre-Treatment	No	0						
PD5882	68	YES	NO	Pre-Treatment	No	0						
PD5883	74	YES	NO	Pre-Treatment	No	0						
PD5884	54	YES	NO	Pre-Treatment	No	0						
PD5885	57	YES	NO	Pre-Treatment	No	0						
PD5886	56	YES	NO	Pre-Treatment	No	0						
PD5887	57	YES	NO	Pre-Treatment	No	0						
PD5888	68	YES	NO	Pre-Treatment	No	0						
PD5889	73	YES	NO	Pre-Treatment	No	0						
PD5890	47	YES	NO	Pre-Treatment	No	0						
PD5891	59	YES	NO	Pre-Treatment	No	0						
PD5892	56	YES	NO	Pre-Treatment	No	0						
PD5893	64	YES	NO	Pre-Treatment	No	0						
PD5894	72	YES	NO	Pre-Treatment	No	0						
PD5895	66	YES	NO	Pre-Treatment	No	0						
PD5896	40	YES	NO	Pre-Treatment	No	0						
PD5897	60	YES	NO	Pre-Treatment	No	0						
PD5898	58	YES	NO	Pre-Treatment	No	0						
PD5899	70	YES	NO	Pre-Treatment	No	0						
PD5900	51	YES	NO	Pre-Treatment	No	0						
PD5901	60	YES	NO	Pre-Treatment	No	0						

SUPPLEMENTARY TABLE S1. PATIENT INFORMATION

Clinical information on each patient age, analysis performed, disease status at the time of sampling is provided. Criteria used to define disease response are as follows: no Response: M-protein decrease <25%. Partial Remission: M-protein decrease >50% <90%. Very Good Partial remission: : M-protein decrease >90% <100%. Complete Remission: Normal serum protein electrophoresis, negative serum immunofixation, bone marrow trephine showing < 5% plasma cells.

SUPPLEMENTARY TABLE S2. SAMPLE INFORMATION

Sample	Sample_type	Patient	HYPER	t{11;14}	t{4;14}	t{14;16}	-1p	+1q	del{12p}	del{13}	-{14q}	-{16q}	Del{17p}
PD4283a	Early	PD4283	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	Subclonal
PD4283c	Late	PD4283	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO
PD4284a	Late	PD4284	NO	YES	NO	NO	YES	NO	YES	Subclonal	YES	YES	YES
PD4284c	Early	PD4284	NO	YES	NO	NO	YES	NO	YES	Subclonal	YES	YES	YES
PD4285a	Early	PD4285	NO	YES	NO	NO	NO	NO	YES	NO	YES	NO	NO
PD4285c	Late	PD4285	NO	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO
PD4286a	Early	PD4286	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD4286c	Late	PD4286	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD4288a	Early	PD4288	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	YES
PD4288c	Late	PD4288	NO	NO	YES	NO	NO	YES	NO	YES	NO	NO	YES
PD4289a	Early	PD4289	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	NO
PD4289c	Late	PD4289	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	NO
PD4289d	Later	PD4289	YES	NO	NO	NO	NO	NO	Subclonal	NO	NO	NO	NO
PD4291a	Early	PD4291	YES	Subclonal	NO	NO	NO	YES	NO	NO	NO	NO	NO
PD4291c	Later	PD4291	YES	Subclonal	NO	NO	NO	YES	NO	NO	NO	NO	Subclonal
PD4292a	Later	PD4292	YES	NO	NO	CN LOH	YES	NO	NO	NO	NO	Subclonal	NO
PD4292c	Later	PD4292	YES	NO	NO	CN LOH	YES	NO	NO	NO	NO	Subclonal	NO
PD4292d	Early	PD4292	YES	NO	NO	CN LOH	YES	NO	NO	NO	NO	Subclonal	NO
PD4293a	Early	PD4293	NO	YES	NO	NO	NO	NO	NO	YES	NO	YES	YES
PD4293c	Late	PD4293	NO	YES	NO	NO	NO	NO	NO	YES	NO	YES	YES
PD4294a	Early	PD4294	NO	YES	NO	NO	NO	YES	NO	YES	NO	YES	NO
PD4294c	Late	PD4294	NO	YES	NO	NO	NO	YES	NO	YES	NO	YES	NO
PD4295a	Early	PD4295	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD4295c	Late	PD4295	NO	YES	NO	NO	NO	NO	Subclonal	NO	NO	NO	NO
PD4296a	Early	PD4296	YES	Subclonal	NO	NO	NO	YES	NO	NO	NO	NO	YES
PD4296c	Late	PD4296	YES	Subclonal	NO	NO	NO	YES	NO	NO	NO	NO	YES
PD4299a	Late	PD4299	YES	NO	NO	YES	NO	NO	NO	NO	NO	Subclonal	NO
PD4299c	Early	PD4299	YES	NO	NO	YES	NO	NO	NO	NO	NO	Subclonal	NO
PD4300a	Early	PD4300	YES	NO	NO	NO	YES	YES	YES	NO	NO	NO	NO
PD4300c	Late	PD4300	YES	NO	NO	NO	YES	YES	YES	NO	NO	NO	NO
PD4301a	Early	PD4301	YES	NO	NO	NO	YES	NO	Subclonal	Subclonal	YES	NO	NO
PD4301d	Late	PD4301	YES	NO	NO	NO	YES	NO	NO	NO	YES	NO	NO
PD5850a	Tumour	PD5850	NO	N/A	NO	N/A	NO	NO	YES	YES	YES	YES	YES
PD5851a	Tumour	PD5851	YES	NO	NO	YES	NO	Subclonal	NO	NO	YES	YES	YES
PD5852a	Tumour	PD5852	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD5853a	Tumour	PD5853	NO	N/A	NO	NO	YES	YES	YES	YES	NO	YES	YES
PD5855a	Tumour	PD5855	YES	NO	NO	YES	NO	NO	YES	NO	NO	NO	YES
PD5856a	Tumour	PD5856	NO	N/A	NO	NO	NO	Subclonal	NO	YES	NO	NO	YES
PD5857a	Tumour	PD5857	NO	N/A	NO	NO	NO	NO	YES	NO	NO	NO	NO
PD5858a	Tumour	PD5858	NO	N/A	NO	NO	YES	NO	YES	YES	NO	YES	YES
PD5859a	Tumour	PD5859	YES	NO	NO	NO	YES	Subclonal	YES	NO	NO	NO	YES
PD5860a	Tumour	PD5860	NO	N/A	NO	YES	NO	YES	YES	YES	YES	YES	YES
PD5861a	Tumour	PD5861	NO	N/A	NO	NO	NO	NO	YES	NO	NO	NO	YES
PD5862a	Tumour	PD5862	NO	N/A	NO	NO	NO	NO	YES	NO	NO	YES	YES
PD5863a	Tumour	PD5863	NO	N/A	NO	YES	YES	YES	YES	YES	NO	NO	YES
PD5864a	Tumour	PD5864	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	YES
PD5865a	Tumour	PD5865	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD5866a	Tumour	PD5866	YES	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO
PD5867a	Tumour	PD5867	NO	N/A	NO	NO	YES	YES	YES	YES	NO	NO	NO
PD5868a	Tumour	PD5868	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD5869a	Tumour	PD5869	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES
PD5870a	Tumour	PD5870	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO
PD5871a	Tumour	PD5871	NO	NO	YES	NO	NO	YES	YES	YES	Subclonal	NO	NO
PD5872a	Tumour	PD5872	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO
PD5873a	Tumour	PD5873	NO	NO	YES	NO	YES	Subclonal	YES	NO	NO	NO	NO
PD5874a	Tumour	PD5874	NO	NO	YES	Subclonal	YES	NO	YES	NO	Subclonal	NO	NO
PD5875a	Tumour	PD5875	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO
PD5876a	Tumour	PD5876	NO	NO	YES	NO	YES	NO	YES	NO	NO	NO	NO
PD5877a	Tumour	PD5877	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD5878a	Tumour	PD5878	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD5879a	Tumour	PD5879	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO
PD5880a	Tumour	PD5880	NO	N/A	NO	NO	NO	NO	NO	NO	NO	YES	YES
PD5881a	Tumour	PD5881	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO
PD5882a	Tumour	PD5882	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO
PD5883a	Tumour	PD5883	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	YES
PD5884a	Tumour	PD5884	NO	N/A	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD5885a	Tumour	PD5885	NO	N/A	NO	NO	NO	NO	NO	NO	CN LOH	NO	NO
PD5886a	Tumour	PD5886	YES	NO	NO	NO	YES	CN LOH	YES	NO	NO	NO	NO
PD5887a	Tumour	PD5887	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD5888a	Tumour	PD5888	YES	NO	NO	YES	NO	NO	Subclonal	NO	NO	NO	NO
PD5889a	Tumour	PD5889	YES	NO	NO	YES	NO	NO	YES	NO	YES	YES	YES
PD5890a	Tumour	PD5890	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD5891a	Tumour	PD5891	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD5892a	Tumour	PD5892	NO	NO	YES	NO	YES	YES	Subclonal	NO	NO	NO	CN LOH
PD5893a	Tumour	PD5893	NO	NO	YES	NO	NO	YES	YES	NO	NO	NO	YES
PD5894a	Tumour	PD5894	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD5895a	Tumour	PD5895	YES	NO	NO	YES	NO	NO	Subclonal	NO	NO	NO	NO
PD5896a	Tumour	PD5896	NO	YES	NO	NO	NO	Subclonal	YES	NO	NO	NO	NO
PD5897a	Tumour	PD5897	YES	NO	NO	NO	NO	NO	NO	NO	YES	YES	YES
PD5898a	Tumour	PD5898	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
PD5899a	Tumour	PD5899	YES	NO	NO	NO	YES	NO	YES	NO	YES	YES	NO
PD5900a	Tumour	PD5900	YES	NO	NO	NO	NO	NO	YES	YES	NO	NO	NO
PD5901a	Tumour	PD5901	YES	NO	NO	NO	YES	NO	YES	NO	YES	YES	NO
PD7181c	Tumour	PD7181	NO	YES	NO	N/A	NO	NO	NO	NO	NO	NO	YES

SUPPLEMENTARY TABLE S3. SEQUENCING METRICS

Sample	Read Length	Reads (PE)	Bases (Gb)	Unmapped reads(%)	Mapped (Gb)	Mapped (%)	Unique mapped (Gb)	Unique mapped (%)	% target covered at 0X	% target covered at 1X	% target covered at 11X	% target covered at 21X	% target covered at 31X	% target covered at 41X	% target covered at 51X	% target covered at 10X	% target covered at 20X	% target covered at 50X	Unique mapped reads on Target (Gb)	Unmapped reads (Gb)	Duplicate reads (Gb)	Mapped reads off target (Gb)		
PD4283a	75	44,476,120	6.76	12.2	5.89	87.13	5.35	90.89	2.85	97.15	87.78	90.2	84.83	79.26	73.18	69.77	50.5	21.35	5.54	0.15	4.50684	0.87	0.54	0.8432
PD4283b	75	64,295,004	9.77	10.57	8.69	88.94	7.93	91.27	2.22	97.78	90.2	97.78	88.81	81.64	73.57	65.09	56.79	26.78	7.56	0.3	5.767489	1.08	0.76	2.1625
PD4283c	75	97,489,311	14.62	10.51	12.83	87.75	10.87	84.68	1.71	98.29	92.69	88.86	85.17	81.3	77.2	55.05	22.99	1.99	8.441642	1.79	1.96	2.4284		
PD4284a	75	54,038,414	8.21	11.83	7.2	87.66	6.31	87.63	2.3	97.7	88.81	81.64	73.57	65.09	56.79	26.78	7.56	0.3	4.861224	1.01	0.89	1.4488		
PD4284b	75	49,303,576	7.49	11.05	6.64	88.61	5.94	89.43	2.32	97.68	89.45	82.83	75.5	67.44	59.11	26.13	5.58	0.11	4.61241	0.85	0.7	1.3276		
PD4284c	75	96,575,925	14.49	11.43	12.56	86.72	10.27	81.75	1.62	98.38	92.5	88.35	84.33	80.11	75.63	52.22	20.53	1.53	7.895576	1.93	2.29	2.3744		
PD4285a	75	52,295,604	7.95	10.67	7.06	88.85	6.21	87.89	2.41	97.59	88.63	81.78	74.04	65.59	57.06	25.91	7.01	0.19	4.751892	0.89	0.85	1.4581		
PD4285b	75	49,662,526	7.55	10.44	6.73	89.15	6.01	89.35	2.47	97.53	89.01	82.41	75.21	67.32	59.2	26.74	5.73	0.1	4.654144	0.82	0.72	1.3559		
PD4285c	75	96,953,578	14.54	10.62	12.74	87.57	10.91	85.67	1.66	98.34	93.13	89.44	86.03	82.49	78.71	56.94	22.26	1.4	8.319966	1.8	1.83	2.59		
PD4286a	75	35,286,978	5.36	12.51	4.66	86.9	3.95	84.77	3.14	96.86	84.99	73.34	60.56	48.61	38.72	14.05	2.93	0.06	3.24295	0.7	0.71	0.7071		
PD4286b	75	58,479,434	8.89	10.67	7.91	88.95	6.68	84.48	2.48	97.52	90.09	84.44	78.35	71.63	64.47	32.54	7.92	0.2	5.25716	0.98	1.23	1.4228		
PD4286c	75	110,054,500	16.51	10.69	14.41	87.27	12.33	85.59	1.62	98.38	93.43	90.04	86.91	83.76	80.43	61.12	28.23	3.04	9.581643	2.1	2.08	2.7484		
PD4288a	75	44,858,266	6.82	11.19	6.03	88.49	5.36	88.79	2.61	97.39	87.86	79.9	70.76	60.96	51.41	20.76	4.99	0.09	4.144888	0.79	0.67	1.2151		
PD4288b	75	91,950,886	13.98	10.68	12.41	88.79	10.73	86.44	2.11	97.89	90.46	85.83	81.49	77.15	72.79	51.69	21.77	2.17	8.16553	1.57	1.68	2.5645		
PD4288c	75	109,646,004	16.45	10.91	14.36	87.3	12.26	85.35	1.31	98.69	93.48	90.04	86.85	83.67	80.32	61.26	27.85	2.51	9.408324	2.09	2.1	2.8517		
PD4289a	75	77,829,323	11.83	10.7	10.51	88.88	8.86	84.22	2.24	97.76	90.35	85.27	80.05	74.44	68.57	41.76	15.53	1.59	6.913458	1.32	1.65	1.9465		
PD4289b	75	61,871,441	9.4	10.57	8.36	88.94	7.22	86.3	1.64	98.36	90.53	85.06	79.3	72.79	65.75	33.57	8.65	0.28	5.49081	1.04	1.14	1.7292		
PD4289c	75	104,587,292	15.69	13.26	13.31	84.82	12.65	95.05	1.66	98.34	92.47	88.06	83.92	79.69	75.23	52.07	20.03	1.32	7.725355	2.38	0.66	4.9246		
PD4289d	75	97,163,323	14.57	10.54	12.89	88.47	12.19	94.55	1.59	98.41	92.9	88.45	84.24	79.87	75.25	51.09	19.83	1.82	7.840608	1.68	0.7	4.3494		
PD4291a	75	25,136,802	3.82	11.81	3.36	87.89	3.18	94.64	3.38	96.62	82.52	66.71	50.11	36.54	26.79	7.52	0.8	0.02	2.454324	0.46	0.18	0.7257		
PD4291b	75	64,750,847	9.84	11.16	8.7	88.43	7.61	87.43	1.86	98.14	90.8	85.7	80.36	74.38	67.9	36.74	10.08	0.39	5.839153	1.14	1.09	1.7708		
PD4291c	75	112,417,072	16.86	11.38	14.63	86.78	12.52	85.54	1.42	98.58	93.58	90.16	86.99	83.87	80.63	62.43	30.03	3.22	9.819436	2.23	2.11	2.7006		
PD4292a	75	68,022,884	10.34	11.88	9.06	87.62	7.93	87.51	2.04	97.96	90.16	84.76	79.02	72.65	65.87	36.09	12.07	0.95	6.117995	1.28	1.13	1.812		
PD4292b	75	49,983,568	7.6	11.31	6.68	87.99	6.01	89.9	1.65	98.35	89.74	83.13	75.68	67.29	58.51	24.68	5.26	0.1	4.541156	0.92	0.67	1.4688		
PD4292c	75	174,800,876	26.22	14.51	21.84	83.29	18.08	82.78	1.04	98.96	94.79	91.62	88.79	86.08	83.34	68.54	39.3	5.68	11.701376	4.38	3.76	6.3786		
PD4292d	75	105,424,559	15.81	11.07	13.91	87.93	13.17	94.71	1.54	98.46	93.18	88.94	85.06	81.12	76.96	54.31	21.53	1.94	8.237835	1.9	0.74	4.9322		
PD4293a	75	41,489,042	6.31	12.95	5.46	86.54	4.92	90.2	2.67	97.33	86.93	77.32	66.55	55.7	45.88	18.19	4.41	0.17	3.835632	0.85	0.54	1.0844		
PD4293b	75	57,618,742	8.76	12.02	7.65	87.32	6.71	87.77	1.87	98.13	89.92	83.98	77.51	70.27	62.55	29.67	7.06	0.17	5.026461	1.11	0.94	1.6835		
PD4293c	75	154,184,261	23.13	10.53	20.42	88.31	15.42	75.51	1.46	98.54	94.09	91.19	88.5	85.87	83.15	68.04	38.5	6.13	11.908866	2.71	5	3.5111		
PD4294a	75	51,352,834	7.81	12.05	6.83	87.48	6.16	90.26	2.33	97.67	88.63	81.36	73.14	64.44	55.83	25.48	7.13	0.25	4.723488	0.98	0.67	1.4365		
PD4294b	75	58,119,223	8.83	11.49	7.76	87.87	6.95	89.5	1.76	98.24	90.45	84.91	78.98	72.32	65.12	32.63	8.24	0.24	5.35428	1.07	0.81	1.5957		
PD4294c	75	95,197,850	14.28	10.86	12.59	88.19	11.95	94.93	1.65	98.35	92.5	87.88	83.47	78.89	74.09	49.8	18.68	1.5	7.565545	1.69	0.64	4.3845		
PD4295a	75	55,083,213	8.37	10.89	7.42	88.67	6.73	90.71	2.21	97.79	89.59	83.42	76.52	68.79	60.74	29.04	8.25	0.29	5.132971	0.95	0.69	1.597		
PD4295b	75	55,820,420	8.48	11.3	7.48	88.11	6.65	88.92	1.94	98.06	90.61	85.09	79.07	72.18	64.65	31.3	7.61	0.2	5.222245	1	0.83	1.4278		
PD4295c	75	185,234,762	27.79	10.05	24.63	88.65	14.37	58.34	1.46	98.54	94.22	91.25	88.54	85.88	83.17	67.37	35.4	4.06	10.919763	3.16	10.26	3.4502		
PD4296a	75	47,704,645	7.25	12.75	6.28	86.54	5.71	91.02	2.26	97.74	88.69	81.18	72.35	62.64	53.11	22.2	5.76	0.18	4.37386	0.97	0.57	1.3361		
PD4296b	75	69,523,994	10.57	11.1	9.35	88.49	8.34	89.2	1.78	98.22	91.04	86.22	81.38	76.07	70.25	40.9	12.24	0.61	6.357582	1.22	1.01	1.9824		
PD4296c	75	175,499,064	26.32	10.95	23.15	87.93	17.75	76.67	1.28	98.72	94.86	92.28	89.94	87.71	85.47	72.91	45.02	8.27	13.4758	3.17	5.4	4.2742		
PD4299a	75	57,107,979	8.68	11.78	7.61	87.63	6.66	87.6	2.08	97.92	89.09	82.63	75.31	67.27	59.09	28.65	8.74	0.51	5.170824	1.07	0.95	1.4892		
PD4299b	75	61,936,223	9.41	10.45	8.38	88.97	7.46	89.09	1.45	98.55	90.72	85.29	79.69	73.43	66.63	34.92	9.27	0.33	5.642744	1.03	0.92	1.8173		
PD4299c	75	93,994,219	14.1	10.63	12.46	88.36	11.62	93.25	1.65	98.35	92.58	87.96	83.5	78.83	73.94	49.01	18.52	1.74	7.595994	1.64	0.84	4.024		
PD4300a	75	43,548,441	6.62	11.93	5.8	87.58	5.24	90.31	2.61	97.39	87.58	78.78	68.69	58.3	48.73	19.88	4.99	0.13	4.036896	0.82	0.56	1.2031		
PD4300b	75	71,088,467	10.81	10.57	9.61	88.92	8.42	87.66	1.51	98.49	91.2	86.45	81.71	76.49	70.77	41.47	12.45	0.61	6.41183	1.2	1.19	2.0082		
PD4300c	75	186,119,493	27.92	10.14	24.73	88.58	17.71	71.61	1.38	98.62	94.76	92.25	89.93	87.72	85.51	73.12	45.5	8.16	13.456058	3.19	7.02	4.2539		
PD4301a	75	47,077,920	7.16	12.78	6.21	86.75	5.45	87.85	2.36	97.64	87.95	79.84	70.56	6										

PD5858b	75	48,727,142	7.31	10	6.39	87.42	5.77	90.32	2.72	97.28	86.92	78.83	70.28	61.51	52.86	21.12	3.46	0.07	3.99284	0.92	0.62	1.7772
PD5859a	75	52,725,272	7.91	9.39	6.96	88.04	6.7	96.16	2.85	97.15	86.54	78.44	70.16	61.87	53.88	23.84	4.67	0.11	4.28398	0.95	0.26	2.416
PD5859b	75	49,275,283	7.39	9.57	6.5	87.91	5.99	92.22	3.07	96.93	86.34	78.16	69.7	61.16	52.83	21.74	3.65	0.07	4.045047	0.89	0.51	1.945
PD5860a	75	52,693,329	7.9	9.44	6.95	87.93	6.71	96.51	2.71	97.29	86.61	78.13	69.32	60.47	52.15	23.01	4.75	0.12	4.208512	0.95	0.24	2.5015
PD5860b	75	60,083,961	9.01	10.47	7.8	86.6	7.01	89.84	2.17	97.83	89.77	83.74	77.18	69.76	61.86	27.97	5.42	0.16	4.767501	1.21	0.79	2.2425
PD5861a	75	57,905,499	8.69	9.03	7.67	88.3	7.42	96.74	2.79	97.21	86.9	79.32	71.64	63.98	56.5	26.41	5.19	0.1	4.497262	1.02	0.25	2.9227
PD5861b	75	53,162,380	7.97	9.84	6.97	87.35	6.3	90.39	2.8	97.2	87.23	79.82	71.97	63.93	55.9	24.38	4.42	0.09	4.30101	1	0.67	1.999
PD5862a	75	59,277,305	8.89	9.6	7.8	87.73	7.48	95.88	2.64	97.36	87.12	79.51	71.78	64.12	56.74	27.49	6.1	0.18	4.675748	1.09	0.32	2.8043
PD5862b	75	59,874,832	8.98	9.96	7.84	87.27	7.09	90.51	2.49	97.51	88.1	81.25	74.18	66.9	59.59	28.83	6	0.14	4.753136	1.14	0.75	2.3369
PD5863a	75	58,736,103	8.81	9.93	7.7	87.42	7.39	95.97	2.56	97.44	87.55	79.86	71.78	63.56	55.68	27	6.62	0.26	4.697823	1.11	0.31	2.6922
PD5863b	75	46,716,517	7.01	9.91	6.13	87.47	5.68	92.66	2.61	97.39	87.13	78.99	70.07	60.8	51.71	19.5	2.99	0.06	3.863536	0.88	0.45	1.8165
PD5864a	75	50,652,902	7.6	9.9	6.64	87.4	6.21	93.57	2.77	97.23	86.44	77.55	68.23	59.08	50.65	22.34	4.86	0.16	4.170636	0.96	0.43	2.0394
PD5864b	75	48,913,343	7.34	9.68	6.44	87.74	5.94	92.23	2.58	97.42	87.52	79.76	71.41	62.6	53.87	21.48	3.5	0.06	4.055238	0.9	0.5	1.8848
PD5865a	75	105,080,065	15.76	9.9	13.81	87.62	12.75	92.33	1.76	98.24	91.8	87.4	83.34	79.21	74.91	52.8	22.07	2.14	8.306625	1.95	1.06	4.4434
PD5865b	75	43,617,788	6.54	10.09	5.71	87.34	5.23	91.53	2.85	97.15	86.23	77.36	67.87	58.2	48.88	17.58	2.52	0.05	3.643218	0.83	0.48	1.5868
PD5866a	75	110,684,161	16.6	9.83	14.56	87.68	13.75	94.48	1.85	98.15	91.7	87.37	83.43	79.42	75.27	53.99	23.5	2.33	8.55525	2.04	0.81	5.1948
PD5866b	75	46,348,319	6.95	9.93	6.08	87.49	5.51	90.51	2.92	97.08	86.61	78.28	69.35	60.16	51.25	19.49	2.9	0.05	3.828348	0.87	0.57	1.6817
PD5867a	75	57,333,226	8.6	10.19	7.49	87.12	7.14	95.3	2.66	97.34	87.27	79.92	72.42	64.8	57.34	27.29	5.71	0.15	4.627434	1.11	0.35	2.5126
PD5867b	75	36,898,546	5.53	10.09	4.83	87.3	4.53	93.75	3.16	96.84	84.23	73.45	62.16	51.14	41.08	12.21	1.33	0.03	3.089913	0.7	0.3	1.4401
PD5868a	75	56,944,441	8.54	9.49	7.49	87.75	7.19	95.91	2.61	97.39	87.32	79.76	71.91	63.86	55.92	25.97	5.85	0.19	4.563493	1.05	0.3	2.6265
PD5868b	75	52,716,350	7.91	9.92	6.92	87.49	6.47	93.47	2.41	97.59	87.99	80.62	72.74	64.44	56.1	23.7	4.13	0.08	4.278611	0.99	0.45	2.1914
PD5869a	75	62,236,146	9.34	9.21	8.28	88.67	7.72	93.24	2.56	97.44	87.91	81.04	74.12	67.11	60.19	31.46	7.96	0.27	5.125308	1.06	0.56	2.5947
PD5869b	75	58,930,039	8.84	10.58	7.33	82.96	6.59	89.85	2.98	97.02	86.38	78.61	70.8	62.96	55.29	24.75	4.54	0.08	4.321063	1.51	0.74	2.2689
PD5870a	75	63,702,012	9.56	9.65	8.43	88.24	7.92	93.9	2.44	97.56	88.41	81.8	75.11	68.23	61.36	32.23	8.16	0.29	5.228784	1.13	0.51	2.6912
PD5870b	75	57,391,385	8.61	10.48	7.16	83.21	6.34	88.57	3.22	96.78	85.6	77.56	69.59	61.81	54.29	24.7	4.72	0.09	4.283304	1.45	0.82	2.0567
PD5871a	75	64,782,815	9.72	9.95	8.54	87.87	8.07	94.52	2.56	97.44	88.45	81.98	75.35	68.42	61.56	32.54	8	0.26	5.218062	1.18	0.47	2.8519
PD5871b	75	64,465,373	9.67	10.78	7.98	82.57	6.98	87.45	3.42	96.58	85.71	78.22	70.96	63.97	57.22	28.94	6.37	0.16	4.710104	1.69	1	2.2699
PD5872a	75	64,789,590	9.72	10.11	8.53	87.75	7.99	93.71	2.5	97.5	88.18	81.58	74.96	68.19	61.5	32.78	8.39	0.35	5.28139	1.19	0.54	2.7086
PD5872b	75	61,847,634	9.28	11	7.64	82.4	6.53	85.46	3.44	96.56	85.06	77.04	69.39	62.11	55.12	26.69	5.56	0.12	4.469132	1.64	1.11	2.0609
PD5873a	75	59,762,650	8.96	9.46	7.92	88.36	7.41	93.51	2.75	97.25	87.59	80.54	73.41	66.26	59.26	30.25	6.96	0.21	4.946175	1.04	0.51	2.4638
PD5873b	75	60,039,108	9.01	10.51	7.47	82.94	6.48	86.71	3.21	96.79	86	78.31	70.69	63.14	55.82	26.12	5.17	0.11	4.43556	1.54	0.99	2.0444
PD5874a	75	58,302,575	8.75	10.45	7.64	87.39	7.16	93.7	2.62	97.38	87.45	80.19	72.72	65.14	57.72	28.03	6.23	0.2	4.747796	1.11	0.48	2.4122
PD5874b	75	59,280,491	8.89	11.02	7.35	82.63	6.37	86.74	3.35	96.65	85.26	77.18	69.39	61.92	54.73	25.96	5.23	0.1	4.391478	1.54	0.98	1.9785
PD5875a	75	81,181,840	12.18	10.07	10.75	88.32	10.09	93.86	1.99	98.01	90.97	85.98	81.16	76.08	70.85	45.2	15.35	0.94	6.878353	1.43	0.66	3.2116
PD5875b	75	84,539,683	12.68	9.9	11.22	88.47	10.21	91.02	1.89	98.11	91.36	86.69	82.3	77.69	72.87	48.3	16.42	0.83	7.131685	1.46	1.01	3.0783
PD5876a	75	55,379,187	8.31	10.39	7.22	86.97	6.87	95.12	2.86	97.14	86.98	79.47	71.88	64.32	56.95	27.41	5.82	0.14	4.602213	1.09	0.35	2.2678
PD5876b	75	62,712,165	9.41	9.83	8.23	87.5	7.7	93.54	2.63	97.37	88.08	81.59	75.1	68.55	62.03	33.36	8	0.21	5.20982	1.18	0.53	2.4902
PD5877a	75	54,892,748	8.23	9.82	7.21	87.52	6.82	94.6	3.02	96.98	86.93	79.53	71.99	64.38	56.9	27.57	6.37	0.21	4.66147	1.02	0.39	2.1585
PD5877b	75	61,794,616	9.27	9.58	8.14	87.82	7.55	92.78	2.86	97.14	87.89	81.46	75.01	68.48	62.04	33.66	8.17	0.22	5.232905	1.13	0.59	2.3171
PD5878a	75	58,117,608	8.72	10.1	7.61	87.34	7.24	95.05	2.82	97.18	87.39	80.26	73.07	65.76	58.55	29.44	7.28	0.28	4.907272	1.11	0.37	2.3327
PD5878b	75	60,848,247	9.13	9.99	7.98	87.41	7.49	93.86	2.63	97.37	88.17	81.89	75.46	68.82	62.13	32.41	7.54	0.21	5.129152	1.15	0.49	2.3608
PD5879a	75	55,038,175	8.26	9.94	7.23	87.6	6.89	95.21	2.78	97.22	87.3	79.84	72.14	64.32	56.68	27.21	6.38	0.23	4.666597	1.03	0.34	2.2234
PD5879b	75	62,394,908	9.36	9.93	8.19	87.56	7.38	90.11	2.49	97.51	88.78	82.73	76.55	70.04	63.45	33.82	7.97	0.22	5.275224	1.17	0.81	2.1048
PD5880a	75	62,291,108	9.34	9.82	8.18	87.57	7.78	95.1	2.96	97.04	87.06	80.09	73.29	66.58	60.05	32.38	8.5	0.33	5.182258	1.16	0.4	2.5977
PD5880b	75	66,456,948	9.97	10.22	8.69	87.16	7.84	90.19	2.78	97.22	88.2	82.09	76.05	69.95	63.91	36.45	9.62	0.31	5.57032	1.28	0.85	2.2697
PD5881a	75	61,199,934	9.18	10.51	7.98	86.98	7.52	94.24	2.74	97.26	87.7	80.81	73.85	66.82	59.95	31.4	8.21	0.39	5.13616	1.2	0.46	2.3838
PD5881b	75	62,989,036	9.45	10.16	8.25	87.27	7.6	92.19	2.57	97.43	88.65	82.55	76.42	70.06	63.62	34.58	8.46	0.24	5.358	1.2	0.65	2.242
PD5882a	75	57,796,669	8.67	10.01	7.59	87.49	7.21	95.12	2.67	97.33	87.78	80.81	73.75	66.53	59.37	29.64	6.92	0.24	4.876123	1.08	0.38	2.3339
PD5882b	75	57,851,627	8.68	9.93	7.6	87.6	7.03	92.47	2.79	97.21	87.74	80.98	74.17	67.28	60.46	31.17	7.02	0.17	4.965289	1.08	0.57	2.0647
PD5883a	75	59,510,536	8.93	9.92	7.82	87.55	7.41	94.84	2.89	97.11	86.9	79.56	72.36	65.31	58.52	31.07	8	0.29	5.022498	1.11	0.41	2.3875

PD5895b	75	54,668,781	8.2	9.72	7.17	87.38	6.76	94.33	3.29	96.71	86.13	78.66	71.32	64.12	57.13	28.02	5.84	0.12	4.609644	1.03	0.41	2.1504
PD5896a	75	54,526,456	8.18	9.99	7.13	87.17	6.77	94.97	3.31	96.69	86.36	79	71.65	64.36	57.25	28.03	5.94	0.14	4.622556	1.05	0.36	2.1474
PD5896b	75	54,696,192	8.2	9.94	7.16	87.27	6.69	93.46	3.37	96.63	86.18	78.71	71.37	64.25	57.32	28.41	5.96	0.12	4.637508	1.04	0.47	2.0525
PD5897a	75	51,519,676	7.73	10.31	6.71	86.89	6.37	94.89	3.21	96.79	85.92	77.91	69.87	61.95	54.3	24.71	4.97	0.11	4.327778	1.02	0.34	2.0422
PD5897b	75	54,708,306	8.21	10.39	7.12	86.73	6.66	93.57	2.95	97.05	86.9	79.63	72.27	64.79	57.44	27.14	5.42	0.12	4.55877	1.09	0.46	2.1012
PD5898a	75	80,004,276	12	9.38	10.69	89.07	10.08	94.28	2.07	97.93	91.19	86.42	81.82	76.92	71.74	45.47	14.92	0.83	6.81912	1.31	0.61	3.2609
PD5898b	75	79,533,759	11.93	9.42	10.62	89.01	9.74	91.7	2.04	97.96	91.23	86.59	82.13	77.37	72.33	46.49	14.79	0.66	6.831636	1.31	0.88	2.9084
PD5899a	75	87,325,082	13.1	9.73	11.62	88.69	10.91	93.91	1.91	98.09	91.46	86.76	82.29	77.66	72.81	48.61	18.2	1.34	7.456985	1.48	0.71	3.453
PD5899b	75	84,307,564	12.65	9.79	11.2	88.57	10.2	91.06	1.93	98.07	91.46	86.91	82.61	78.12	73.4	48.94	16.71	0.85	7.19202	1.45	1	3.008
PD5900a	75	89,600,889	13.44	9.71	11.9	88.52	11.1	93.26	2	98	90.81	85.87	81.19	76.4	71.5	47.89	18.18	1.34	7.42923	1.54	0.8	3.6708
PD5900b	75	104,701,706	15.71	9.36	13.95	88.85	12.45	89.22	1.81	98.19	91.63	87.22	83.22	79.2	75.03	54.08	22.44	1.57	8.24688	1.76	1.5	4.2031
PD5901a	75	48,902,750	7.34	10.03	6.45	87.96	6.19	95.98	2.7	97.3	87.15	79.05	70.46	61.66	53.12	22.38	4.24	0.11	4.146681	0.89	0.26	2.0433
PD5901b	75	54,681,493	8.2	9.71	7.24	88.29	6.89	95.15	2.54	97.46	88.37	81.71	74.74	67.37	59.9	28.41	5.8	0.13	4.714827	0.96	0.35	2.1752

SUPPLEMENTARY TABLE S4. GENES MUTATED AT A SIGNIFICANT RECURRENCE RATE IN THE STUDY

gene_name	cds_id	n_syn	n_mis	n_non	n_splice	n_ind	wMIS1	wNON1	wSPLICE1	wIND	pMIS1	pNON1	pSPLICE1	pIND	p ^T	qMIS1	qNON1	qSPLICE1	qIND	q ^T	p_ALL	q_ALL		
FAAH6C	CCDS8956	0	4	1	0	6	52.4583868	272.8979405	0	1475.9221	1.05E-05	0.00238664	1	1.11E-16	0.79225894	0.00424947	1	1	2.24E-12	1	0	0	0	
KRAS	CCDS8703	1	17	0	0	0	497.3481541	0	0	0	0.9441209	0.9544059	1	0.00779084	1	1	1	1	1	1	0	0		
NRAS	CCDS8777	0	17	0	0	0	0	79.7140551	0	0	0	0.9454777	0.9628081	1	0.0077563	0	1	1	1	1	0	0		
TP53	CCDS11118	0	6	0	2	2	75.02360765	0	0	566.0895	471.525234	2.39E-10	0.91970563	3.80E-06	8.97E-06	0.80642394	1.21E-06	1	0.07674329	0.09052521	1	1.11E-16	5.60E-13	
BRAF	CCDS5863	0	9	0	0	1	61.55593467	0	0	121.240876	5.76E-14	0.87130564	0.90481193	0.0082112	0.74842838	3.88E-10	1	1	1	1	3.78E-12	1.53E-08		
SP140	CCDS42831	0	1	1	1	2	6.122541096	77.8536919	92.8913941	211.617214	0.16252047	0.00945206	0.00777582	4.44E-05	0.73903383	1	1	1	1	0.29859238	0.00334232			
LTB	CCDS4703	0	0	1	1	1	0	487.6227296	816.158033	385.707641	0.74928583	0.00127168	0.00072984	0.00258928	0.80356939	1	1	1	1	3.65E-06	0.00105372			
ROBO1	CCDS54611	0	2	2	0	1	1.285672973	75.78184799	0	56.105921	0.04578575	0.00205338	0.0025647	0.87640823	0.01747883	0.63991994	1	1	1	1	1	0.0015262	0.38504793	
TGDS	CCDS9471	0	1	1	0	1	16.24541212	207.6474924	0	261.083692	0.05445381	0.00321489	0.92362691	0.00382286	0.83822051	1	1	1	1	1	0.00039835	0.81299243		
SNX7	CCDS7575	0	1	1	1	0	0.113740542	167.5917414	313.377588	0	0.0813106	0.004064	0.00205338	1	0.81172928	0.0025647	0.63991994	1	1	1	1	1	0.00040279	0.81299243
MPEG1	CCDS41650	0	3	1	0	0	23.04622258	115.54144362	0	0	0.00029761	0.00612081	1	1	0.73401115	0.35448671	1	1	1	1	1	0.0008577	1	
DHX32	CCDS7652	0	1	1	1	0	7.27637529	97.25342739	240.023212	0	0.13412251	0.0073918	0.00274478	1	0.75159664	1	1	1	1	1	0.00121536	1		
RYR2	CCDS5691	0	7	1	0	0	7.37468322	14.98863043	0	0	6.78E-05	0.05961597	0.768475	1	0.40252957	0.12441652	1	1	1	1	1	0.016563	1	
NFKBIA	CCDS5568	0	0	1	1	0	0	0	222.0708485	439.586449	0	0.00026350	0.00027764	0.000264	1	1	1	1	1	1	0.0002223	1		
EGR3	CCDS4296	1	4	0	0	0	35.19915591	0	0	0	5.33E-06	0.9534021	1	0.0478952	0.792404	1	1	1	1	1	0.00026273	1		
F5P12	CCDS54426	1	6	2	0	0	4.075023735	19.88249469	0	0	0.000187777	0.00326116	0.80895236	1	0.39093683	0.798664127	1	1	1	1	1	0.00039165	1	
SI	CCDS3196	2	4	1	0	0	12.18710947	36.139591	0	0	0.00037267	0.02219877	0.84327658	1	0.39039398	1	1	1	1	1	0.00238724	1		
NECAB3	CCDS42866	1	2	0	1	0	24.58188454	0	211.623586	0	0.000274334	0.91813575	0.00314899	1	0.03089704	0.8789151	1	1	1	1	1	0.002397851	1	
CDA3Y	CCDS45685	2	0	2	0	0	0	317.5195056	0	0	0.62822180	1.27E-05	0.93249918	1	0.00125721	0.25637899	1	1	1	1	1	0.00399649	1	
EIF4G2	CCDS31428	0	0	0	2	0	0	0	229.023649	0	0.55881334	0.86788335	2.52E-05	1	0.73527354	1	1	1	1	1	0.00668211	1		
ZFHX4	CCDS47878	2	5	1	0	0	7.345664197	22.1774785	0	0	0.00077405	0.0383747	0.93236995	1	0.02828494	0.55797874	1	1	1	1	1	0.00756105	1	
CND1	CCDS8191	4	3	0	0	0	48.06244759	0	0	0	3.09E-05	0.9372003	0.95301741	1	2.65E-06	0.08918214	1	1	1	1	1	0.00053434	0.00779102	
TRAF3	CCDS9975	0	0	1	0	1	0	132.8750815	0	165.114573	0.63229353	0.00524238	0.93159532	0.0060381	0.75593733	1	1	1	1	1	0.00792582	1		
CYLD	CCDS45482	0	0	0	1	1	0	155.756528	98.0280349	0	0.55479807	0.87103162	0.00440356	0.01014931	0.72975912	1	1	1	1	1	0.01021797	1		
LRRK1A	CCDS54973	0	1	0	1	1	3.877634642	65.8401132	67.3372279	0.26814166	0.8494124	0.011381	0.0147409	0.66138697	1	1	1	1	1	0.01026682	1			
USP29	CCDS59124	1	0	2	0	0	0	169.6764137	0	0	0	0.000274334	0.91813575	0.00314899	1	0.03089704	0.8789151	1	1	1	1	1	0.002397851	1
ASXL2	CCDS1691	1	0	2	0	0	0	161.0376684	0	0	0.52711509	5.26E-05	0.87764219	1	0.07975881	0.35401053	1	1	1	1	1	0.0151157	1	
ZNF607	CCDS33906	0	2	1	0	0	0	15.56813988	91.19676184	0	0	0.00713282	0.00793553	0.95807865	1	0.78546252	1	1	1	1	1	0.01214683	1	
SPATA31D1	CCDS47986	1	3	1	0	0	0	10.28312723	44.48236298	0	0	0.00342404	0.01760387	0.96355774	1	0.10295874	0.98453797	1	1	1	1	1	0.01320091	1
AGMO	CCDS34604	0	3	0	0	0	0	38.0711558	0	0	0	6.35E-05	0.90735324	0.91915642	1	0.81687338	0.12441652	1	1	1	1	1	0.01323949	1
MECOM	CCDS54670	0	4	0	0	0	0	19.02544709	0	0	0	6.38E-05	0.86655751	0.90801794	1	0.70920584	0.12441652	1	1	1	1	1	0.01323949	1
FBXL2	CCDS2658	0	3	0	0	0	0	37.37141804	0	0	0	6.73E-05	0.906533978	0.91445304	1	0.79472746	0.12441652	1	1	1	1	1	0.01375889	1
SP3	CCDS2254	0	2	1	0	0	0	13.83950325	83.33973957	0	0	0.0091202	0.00876621	0.94151601	1	0.74378227	1	1	1	1	1	0.01558046	1	
PEG3	CCDS12948	0	3	1	0	0	0	9.39354037	42.55884134	0	0	0	0.00447844	0.01849369	0.94463011	1	0.64606571	1	1	1	1	1	0.01598031	1
OR651	CCDS32038	0	1	1	0	0	0	16.85753132	390.1224296	0	0	0	0.05223468	0.00161897	0.97666029	1	0.81921939	1	1	1	1	1	0.01622077	1
RP15	CCDS741	0	1	0	1	1	0	17.74565963	0	338.133063	0	0	0.04930362	0.92927528	0.00189064	1	0.850022	1	1	1	1	1	0.01739095	1