Mutational screening of newly diagnosed multiple myeloma patients by deep targeted sequencing

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doi:10.3324/haematol.2018.188839

Supplementary Data

Table S1: Genes included in the panel sequencing for variant detection.

ACTG1	ATM	B2M	BAGE2	BIRC2	BIRC3	BRAF
CARD11	CCNB1	CCND1	CCNT1	CDK4	CDK7	CDKN1B
CDKN2A	CDKN2C	CRBN	CSNK2A1	CUL4A	CUL4B	CXCR4
CYLD	DIS3	EGFR	EGR1	FAM46C	FGFR3	GRB2
IDH1	IDH2	IDH3A	IFNGR2	IGF1R	IKZF1	IKZF3
IL6	IL6R	IL6ST	IRF4	JAK2	KDM6A	KRAS
MAF	MAFB	MAP3K14	MAX	MYC	MYD88	NFKBIB
NR3C1	NRAS	PRDM1	PSMA1	PSMB5	PSMB8	PSMB9
PSMD1	PTPN11	RASA2	RB1	RIPK1	RIPK4	SHC1
SP140	SRF	STAT3	TGFBR2	TLR4	TNFRSF13B	TNFRSF21
TNFSF9	TP53	TRAF2	TRAF3	TRAF3IP1	WHSC1	XBP1

Table S2: List of genes grouped by pathway.

NFκB		**RAS**	**CEREBLON**	**CYCLIN**	**MYC**
BIRC2	RIPK4	BRAF	CRBN	CCNB1	MAX
BIRC3	TLR4	EGFR	CUL4A	CCND1	MYC
CARD11	TNFRSF13B	FGFR3	CUL4B	CCNT1	PRDM1
CYLD	TNFRSF21	IGF1R	IKZF1	CDK4	XBP1
MAP3K14	TNFSF9	KRAS	IKZF3	CDK7	
MYD88	TRAF2	NRAS	IRF4	CDKN1B	
NFKBIB	TRAF3	RASA2	MYC	CDKN2A	
RIPK1	TRAF3IP1			CDKN2C	

Table S3: 168 detected mutations and annotation.

SAMPLE	GENE	FUNC	Gtype	LOC	PTEIN	POS_COV	VAR_COV	VRF(%)	GERM	SIFT	POLYPHEN	COSMIC	dbSNP
2	IDH2	UTR 3'	G/A	UTR 3'	_	1692	823	49%	yes	_	_		
3	NRAS	missense	G/T	exonic	Q61K	91	45	49%	yes	deleterious	beningn	**1**	**1**
7	ATM	missense	T/C	exonic	L1444P	436	47	11%		deleterious	probably_damaging		
7	DIS3	missense	A/G	exonic	F775L	1898	212	11%		deleterious	probably_damaging		
9	NRAS	missense	C/G	exonic	G12A	2759	383	14%	yes	deleterious	beningn	1	1
10	DIS3	missense	C/G	exonic	R780T	220	86	39%		deleterious	probably_damaging	1	
11	NRAS	missense	T/C	exonic	Q61R	509	132	26%		tolerated	beningn	1	1
11	ACTG1	missense	C/T	exonic	E3K	720	162	23%		tolerated	beningn		
13	ACTG1	missense	A/G	exonic	V35A	363	117	32%		deleterious	probably_damaging		
13	IRF4	missense	C/T	exonic	A341V	658	311	47%		deleterious	probably_damaging		1
13	KRAS	missense	T/G	exonic	Q61H	935	370	40%		deleterious	beningn	1	1
13	CUL4A	missense	G/A	exonic	E546K	1045	432	41%		deleterious	beningn		
16	CYLD	missense	T/A	exonic	F352I	433	21	5%		deleterious	beningn		
16	TLR4	missense	G/A	exonic	C281Y	116	57	49%		deleterious	probably_damaging		1
16	ATM	missense	C/T	exonic	S333F	204	83	41%		deleterious	beningn		1
17	KRAS	missense	C/T	exonic	G13D	783	341	44%		deleterious	probably_damaging	1	1
19	SP140	splice	T/C	splice	_	219	83	37%		_	_		
21	NRAS	missense	G/T	exonic	Q61K	50	20	40%		deleterious	beningn	1	1
24	DIS3	missense	C/T	exonic	E501K	240	20	8%	yes	deleterious	probably_damaging		
24	DIS3	missense	G/C	exonic	F120L	75	40	53%	yes	deleterious	probably_damaging		
24	IDH2	missense	G/A	exonic	T435M	608	398	65%	yes	tolerated	beningn		1
30	TRAF3IP1	missense	A/G	exonic	N351D	162	20	12%		tolerated	beningn		
30	ACTG1	missense	G/C	exonic	A29G	623	65	10%		deleterious	probably_damaging		1
32	BRAF	missense	C/T	exonic	D594N	307	79	26%		deleterious	probably_damaging	1	
32	TP53	missense	G/A	exonic	R273C	563	164	29%		deleterious	probably_damaging	1	1
32	KRAS	UTR 3'	A/C	UTR 3'	_	1489	407	27%		_	_		
32	DIS3	missense	A/C	exonic	Y782D	1969	851	43%		deleterious	probably_damaging		
33	KRAS	missense	T/A	exonic	Q61H	1590	212	13%		deleterious	beningn	1	1
33	DIS3	missense		exonic	P635S	516	326	63%		tolerated	beningn	1	?
34	RIPK4	missense	G/T	exonic	N498K	1771	38	2%		deleterious	probably_damaging		

SAMPLE	GENE	FUNC	Gtype	LOC	PTEIN	POS_COV	VAR_COV	VRF(%)	GERM	SIFT	POLYPHEN	COSMIC	dbSNP
34	IDH3A	missense	T/A	exonic	D139E	409	217	53%		deleterious	0.755	1	1
36	NR3C1	missense	C/T	exonic	A229T	232	109	47%		tolerated	beningn		1
36	TP53	missense	A/G	exonic	Y126H	853	158	19%		deleterious	probably_damaging	1	
36	RB1	missense	G/C	exonic	A59P	214	181	85%		tolerated	beningn		1
36	MYC	UTR 5'	C/T	UTR 5'	_	409	209	51%		_	_		1
39	GRB2	missense	C/G	exonic	R112P	401	143	36%		deleterious	probably_damaging	1	
39	IL6	missense	G/A	exonic	E200K	689	193	28%		deleterious	beningn		
40	DIS3	missense	T/C	exonic	D479G	989	127	13%	yes	deleterious	probably_damaging	1	
40	TP53	missense	T/A	exonic	D208V	915	324	35%	yes	deleterious	probably_damaging	1	
40	TP53	nonsense	C/A	exonic	E204*	918	326	36%	yes	_	_	1	
42	DIS3	missense	C/A	exonic	D958Y	139	33	24%		deleterious	probably_damaging		
42	DIS3	missense	G/A	exonic	R820W	699	98	14%		deleterious	probably_damaging		1
42	WHSC1	missense	A/C	exonic	S421R	357	166	46%		tolerated	beningn		
42	DIS3	missense	C/T	exonic	G249E	1125	226	20%		deleterious	probably_damaging		1
45	BIRC2	missense	C/T	exonic	P500S	319	173	54%		tolerated	beningn		1
47	CYLD	missense	C/G	exonic	T386R	183	53	29%		deleterious	probably_damaging		1
47	ATM	missense	C/G	exonic	S333F	195	86	44%		deleterious	beningn		1
47	ATM	missense	A/T	exonic	D1853V	134	100	75%		deleterious	beningn	1	1
48	BRAF	missense	C/T	exonic	G466E	440	24	5%		deleterious	probably_damaging	1	1
48	TRAF3	nonsense	G/T	exonic	E332*	254	57	22%		_	_		
48	CDKN1B	missense	T/C	exonic	I119T	741	324	44%		tolerated	beningn		1
48	RIPK4	missense	T/A	exonic	D669V	1436	688	48%		deleterious	probably_damaging		
55	NRAS	missense	C/T	exonic	G12D	757	376	50%	yes	deleterious	beningn	1	1
62	BRAF	missense	C/G	exonic	G469A	1081	75	7%		deleterious	probably_damaging	1	1
62	PSMA1	UTR 3'	A/G	UTR 3'	_	405	155	38%		_	_		
62	KRAS	missense	G/T	exonic	A18D	937	389	42%		deleterious	probably_damaging	1	
65	NRAS	missense	C/G	exonic	G12A	2827	2073	73%		deleterious	beningn	1	1
65	TRAF2	missense	G/A	exonic	D488N	3862	2535	66%		deleterious	probably_damaging		1
65	CDK7	missense	A/G	exonic	D16G	5199	3249	63%		deleterious	probably_damaging		
70	ATM	missense	C/G	exonic	L2379V	2331	1145	50%		deleterious	beningn		
73	FGFR3	missense	G/T	exonic	G377C	552	67	12%		tolerated	beningn		1
73	RASA2	missense	C/G	exonic	F585L	995	95	10%		deleterious	probably_damaging		
76	TRAF3	missense	G/C	exonic	K453N	604	46	8%		deleterious	probably_damaging		
76	TRAF3	missense	G/A	exonic	G416E	968	60	6%		deleterious	probably_damaging		
76	WHSC1	missense	G/C	exonic	D81H	862	65	8%		deleterious	probably_damaging		
76	TP53	missense	C/G	exonic	K139N	2129	68	3%		deleterious	probably_damaging	1	

SAMPLE	GENE	FUNC	Gtype	LOC	PTEIN	POS_COV	VAR_COV	VRF(%)	GERM	SIFT	POLYPHEN	COSMIC	dbSNP
76	CCNT1	missense	G/A	exonic	S292L	860	69	8%		tolerated	probably_damaging		
76	TRAF3	missense	C/G	exonic	F445L	888	116	13%		deleterious	probably_damaging		
76	TRAF2	missense	C/T	exonic	H307Y	2812	212	7%		deleterious	probably_damaging		
76	CUL4B	missense	C/G	exonic	E840Q	1521	495	33%		deleterious	probably_damaging		
76	B2M	missense	C/G	exonic	I21M	1180	522	44%		deleterious	beningn		
76	BRAF	missense	G/A	exonic	S133L	1840	789	43%		deleterious	beningn		
76	IKZF3	missense	C/T	exonic	M58I	1975	836	42%		tolerated	beningn		
78	TNFSF9	missense	C/A	exonic	R150Q	518	237	46%		tolerated	beningn		
79	DIS3	missense	T/C	exonic	E196G	292	20	6%		deleterious	probably_damaging		
79	FAM46C	missense	G/T	exonic	M215I	700	35	5%		deleterious	beningn		
79	KRAS	missense	T/G	exonic	K117N	453	37	8%		deleterious	probably_damaging	1	
79	KRAS	missense	T/A	exonic	Q61L	1701	500	29%		deleterious	probably_damaging	1	1
86	CDKN1B	stoploss	A/T	exonic	*199Y	574	143	25%		_	_		
86	PSMB9	missense	C/T	exonic	R163C	438	166	38%		deleterious	probably_damaging		
86	MYC	missense	C/A	exonic	H302Q	362	182	50%		deleterious	probably_damaging		1
89	TP53	missense	A/T	exonic	N345K	250	20	8%		deleterious	probably_damaging	1	
96	CYLD	missense	C/G	exonic	Q820E	785	50	6%		deleterious	beningn	1	
96	BIRC3	missense	A/G	exonic	D241G	1290	592	46%		tolerated	beningn		
96	IFNGR2	missense	C/T	exonic	T299I	1272	619	49%		deleterious	beningn		
101	WHSC1	missense	A/C	exonic	T569P	349	23	7%		deleterious	probably_damaging		
101	RASA2	stoploss	G/C	exonic	*850Y	266	29	11%		_	_		
101	KDM6A	nonsense	G/A	exonic	W127*	317	65	21%		_	_		
101	RB1	nonsense	G/A	exonic	W681*	2250	278	13%		_	_		
102	IRF4	missense	G/T	exonic	C214F	1040	482	46%		tolerated	beningn		
103	GRB2	missense	C/T	exonic	A197T	244	114	47%		tolerated	beningn		
103	KRAS	missense	T/G	exonic	Q61H	2938	389	13%		deleterious	beningn	1	1
105	DIS3	missense	A/T	exonic	Y753N	2325	49	2%		deleterious	probably_damaging		
105	DIS3	missense	C/T	exonic	E126K	850	491	58%		deleterious	probably_damaging		
105	KRAS	missense	A/G	exonic	Q61H	5265	1633	32%		deleterious	beningn	1	1
153	B2M	UTR 5'	C/A	UTR 5'	_	640	134	21%		_	_		
153	CSNK2A1	splice	T/C	splice	_	595	284	48%		_	_		
157	IGF1R	missense	A/G	exonic	N427S	691	21	3%		tolerated	beningn		
157	BIRC3	missense	G/C	exonic	G127R	1006	125	12%		tolerated	beningn		
159	IGF1R	missense	G/A	exonic	M1082I	1472	108	7%		deleterious	probably_damaging		
159	DIS3	missense	C/T	exonic	R689Q	408	346	85%		deleterious	probably_damaging	1	
168	BRAF	missense	A/T	exonic	T546S	969	29	3%	yes	c.1636A>T			

SAMPLE	GENE	FUNC	Gtype	LOC	PTEIN	POS_COV	VAR_COV	VRF(%)	GERM	SIFT	POLYPHEN	COSMIC	dbSNP
168	KRAS	missense	C/T	exonic	G13D	1174	106	9%	yes	deleterious	probably_damaging	1	1
168	KRAS	missense	A/G	exonic	Q61H	3019	393	13%	yes	deleterious	beningn	1	1
169	ATM	missense	T/C	exonic	I144T	974	30	3%		deleterious	probably_damaging		
169	XBP1	missense	C/G	exonic	G315A	2625	63	3%		tolerated	probably_damaging		
169	TRAF2	missense	G/C	exonic	R393P	1137	66	6%		deleterious	probably_damaging		
169	MAF	missense	T/C	exonic	N275D	1039	78	8%		deleterious	probably_damaging		
169	IRF4	missense	G/C	exonic	D106H	3006	81	3%		deleterious	probably_damaging		
169	DIS3	missense	C/T	exonic	V198I	1419	614	43%		tolerated	beningn		
172	RB1	nonsense	A/T	exonic	K722*	344	172	50%		_	_		
172	KRAS	missense	C/A	exonic	G12V	737	293	40%		deleterious	probably_damaging	1	1
172	CDKN2A	missense	C/T	exonic	A148T	2259	1107	49%		deleterious	probably_damaging		
177	NRAS	missense	G/T	exonic	Q61K	883	43	5%		deleterious	beningn	1	1
177	NRAS	missense	C/G	exonic	G12A	1552	179	12%		deleterious	beningn	1	1
177	PRDM1	missense	T/C	exonic	L784P	1127	559	49%		deleterious	probably_damaging		
185	NRAS	missense	C/G	exonic	G13R	803	20	2%		deleterious	probably_damaging	1	1
185	CARD11	missense	C/T	exonic	V903I	2666	1148	44%		deleterious	beningn		1
189	KRAS	missense	C/G	exonic	G12R	1553	193	12%		deleterious	beningn	**1**	**1**
189	STAT3	missense	G/A	exonic	L207F	3618	577	18%		tolerated	probably_damaging		
190	MAX	missense	C/T	exonic	R36K	609	59	10%		deleterious	probably_damaging	1	
190	MAX	missense	C/A	exonic	R35L	600	127	21%		deleterious	probably_damaging	1	
190	MAX	missense	T/A	exonic	E32V	565	146	26%		deleterious	probably_damaging		
190	PSMB9	missense	G/A	exonic	E112K	2885	1399	48%		deleterious	probably_damaging	1	
227	FAM46C	missense		exonic	A297T	413	314	76%		tolerated	beningn	1	
230	TGFBR2	UTR 5'	G/A	UTR 5'	_	174	66	38%		_	_		
230	IRF4	missense	G/C	exonic	K59N	3032	113	4%		deleterious	probably_damaging		
236	DIS3	missense	C/G	exonic	D479H	1335	55	4%		deleterious	probably_damaging		
236	DIS3	missense	C/G	exonic	D487H	1367	55	4%		deleterious	probably_damaging		
236	MAP3K14	missense	C/T	exonic	R404H	1424	146	10%		tolerated	beningn		1
236	DIS3	missense	G/T	exonic	D479E	1495	308	21%		deleterious	probably_damaging		
239	FAM46C	missense	G/A	exonic	R151H	1147	255	22%		deleterious	probably_damaging		
240	NRAS	missense	C/T	exonic	G12D	3166	418	13%	yes	deleterious	beningn	1	1
252	ATM	missense	A/T	exonic	T2947S	783	38	5%	yes	deleterious	probably_damaging	1	
252	TP53	missense	T/C	exonic	Y236C	5327	257	5%	yes	deleterious	probably_damaging	1	
257	NRAS	missense	G/C	exonic	Q61E	285	21	7%	yes	deleterious	beningn	1	1
257	NRAS	missense	C/G	exonic	G12A	1228	68	6%	yes	deleterious	beningn	1	1
257	IFNGR2	missense	C/T	exonic	R39C	10347	3757	37%	yes	deleterious	probably_damaging		

SAMPLE	GENE	FUNC	Gtype	LOC	PTEIN	POS_COV	VAR_COV	VRF(%)	GERM	SIFT	POLYPHEN	COSMIC	dbSNP
268	IL6	missense	A/C	exonic		333	176	35%		?	?		1
268	FGFR3	missense	G/A	exonic	V790M	675	326	48%		deleterious	probably_damaging		1
268	IGF1R	missense	T/C	exonic	Y203H	1572	758	48%		tolerated	beningn		
268	NRAS	missense	C/G	exonic	G13R	1865	928	50%		deleterious	probably_damaging	1	1
268	IFNGR2	missense	G/C	exonic		3911	1889	48%		deleterious	probably_damaging	1	1
269	KRAS	missense	A/C	exonic	Y71D	979	25	3%		deleterious	probably_damaging		
269	KRAS	UTR 3'	C/G	UTR 3'	_	5276	774	15%		_	_		
269	KRAS	missense	G/C	exonic	Q61E	11405	4133	37%		deleterious	beningn	1	1
271	KRAS	missense	C/T	exonic	G13D	1447	609	42%		deleterious	possibly_damaging	1	1
271	FGFR3	missense	A/G	exonic	Y305C	1921	822	43%		deleterious	probably_damaging		
275	KRAS	missense	C/A	exonic	G12C	2179	479	22%		deleterious	probably_damaging	1	1
282	KRAS	missense	T/A	exonic	Q61H	6074	637	10%		deleterious	beningn	1	1
282	PSMB9	missense	G/A	exonic	V32I	1796	828	46%		tolerated	probably_damaging		
283	TRAF3	missense	C/T	exonic	H136Y	677	76	11%		deleterious	probably_damaging		
283	BRAF	missense	A/T	exonic	V600E	947	345	36%		deleterious	probably_damaging	1	1
294	NRAS	missense	T/C	exonic	Q61R	85	35	41%		deleterious	beningn	1	1
294	TNFRSF13B	missense	G/A	exonic	P205S	3759	1871	50%		tolerated	beningn		
298	KRAS	missense	T/A	exonic	Q61H	3704	347	9%		deleterious	beningn	1	1
303	KRAS	missense	G/T	exonic	Q22K	776	92	12%		deleterious	probably_damaging	1	1
303	TP53	missense	T/G	exonic	I251L	982	144	15%		deleterious	probably_damaging	1	1
303	PSMB8	missense	C/T	exonic	R11Q	1666	207	12%		tolerated	beningn	1	
303	IFNGR2	missense	T/C	exonic	I223T	1038	290	28%		tolerated	beningn		
303	CARD11	missense	C/T	exonic	R331H	1225	441	36%		tolerated	probably_damaging		
307	BRAF	missense	T/G	exonic	K601T	578	20	3%		deleterious	beningn		
307	PRDM1	missense	T/G	exonic	L676R	1616	259	16%		deleterious	probably_damaging		
307	DIS3	missense	A/T	exonic	Y782N	3619	2427	68%		deleterious	probably_damaging		
309	BRAF	missense	C/T	exonic	D594N	566	70	12%		deleterious	probably_damaging	1	
309	DIS3	missense	C/G	exonic	D487H	1478	289	20%		deleterious	probably_damaging		
312	TNFRSF21	missense	T/C	exonic	N527S	574	180	31%		tolerated	beningn		1
316	WHSC1	missense	G/C	exonic	K1351N	1084	532	49%		deleterious	unknown		

Figure S1: Location of detected mutations in the most recurrently mutated genes.