

HICF1 - Final Report v2

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Univariate Analysis

Table 1: Univariate Analysis against MRD outcome

	p.value	uncorrected	corrected.p.value	corrected	MRDneg0	MRDpos1	MRDneg1	sum	testused
TP53_ALL	0.00004	***	0.0004	***	105	19	2	209	Fisher's Exact Test
TP53_mut	0.00001	***	0.0002	***	107	15	0	209	Fisher's Exact Test
TP53_bi	0.009	**	0.019	*	106	9	1	209	Fisher's Exact Test
ATM_ALL	0.002	**	0.006	**	83	44	24	209	Fisher's Exact Test
ATM_del	0.0005	***	0.003	**	98	28	9	209	Fisher's Exact Test
BIRC3_ALL	0.094	trend	0.122	n.s.	94	22	13	209	Fisher's Exact Test
BIRC3_del	0.002	**	0.006	**	101	21	6	209	Fisher's Exact Test
ATM_bi	0.002	**	0.006	**	102	19	5	209	Fisher's Exact Test
BIRC3_bi	0.360	n.s.	0.432	n.s.	106	3	1	209	Fisher's Exact Test
X11q_mono	0.046	*	0.089	trend	104	10	3	209	Fisher's Exact Test
ATM_mono	0.836	n.s.	0.836	n.s.	93	12	14	209	Fisher's Exact Test
BIRC3_mono	0.066	trend	0.095	trend	100	1	7	209	Fisher's Exact Test
NOTCH1_mut	0.069	trend	0.095	trend	88	9	19	209	Fisher's Exact Test
SF3B1_mut	0.415	n.s.	0.467	n.s.	85	26	22	209	Fisher's Exact Test
Trisomy_12	0.002	**	0.006	**	82	8	25	209	Fisher's Exact Test
SAMHD1_ALL	0.054	trend	0.089	trend	105	8	2	209	Fisher's Exact Test
Subclones	0.050	trend	0.089	trend					Wilcoxon Test
Total_num_CNAs	0.483	n.s.	0.511	n.s.					Wilcoxon Test

Associations

Table 2: Uncorrected p-values for association between genetic lesions

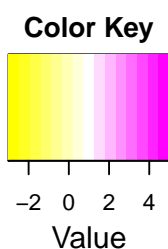
p	variables	TP53_ALL	TP53_del	TP53_cnLOH	TP53_mut	ATM_ALL	ATM_mut	ATM_del	ATM_cnLOH	BIRC3_ALL	BIRC3_mut	BIRC3_del	NOTCH1_mut	SF3B1_mut	X6q-delALL	X13q-
p 1	TP53_ALL															
p 2	TP53_del		0	0.001	0	0	0.510	0.571	0.498	1	0.411	0.343	1	0.593	0.386	0.4
p 3	TP53_cnLOH			1			0.274	0.530	0.429	1	1	0.422	1	0.642	0.634	1
p 4	TP53_mut					0	1	0.632	0.505	1	1	1	1	1	1	1
p 5	ATM_ALL				0.005	0.002	0.173	0.186	0.275	1	0.631	0.087	0.642	0.189	0.181	1
p 6	ATM_mut					0	0.642	0.595	0.527	1	0.505	0.183	1	0.429	0.416	1
p 7	ATM_del							0	0	0.031	0.001	0	0.373	0	0	0.03
p 8	ATM_cnLOH								0.003	0.011	0	0.111	0.197	0.017	0	0.6
p 9	BIRC3_ALL									1	0.283	0	0.018	0	0	0.00
p 10	BIRC3_mut										1	1	1	1	0	1
p 11	BIRC3_del											0.277	1	0.413	0.650	1
p 12	NOTCH1_mut												0	0	0	0.00
p 13	SF3B1_mut													0.042	1	0
p 14	X6q-delALL															0
p 15	X13q-ALL															1
p 16	Trisomy_12															0
p 17	Trisomy_18															0
p 18	Trisomy_19															0
p 19	XPO1_gain															0
p 20	SAMHD1-ALL															0
p 21	MYD88_mut															0
p 22	MED12mutation															0
p 23	X8q-ALL															0
p 24	Subclones															0
p 25	Totalnum.CNAs															1

Table 3: Corrected p-values for association between genetic lesions

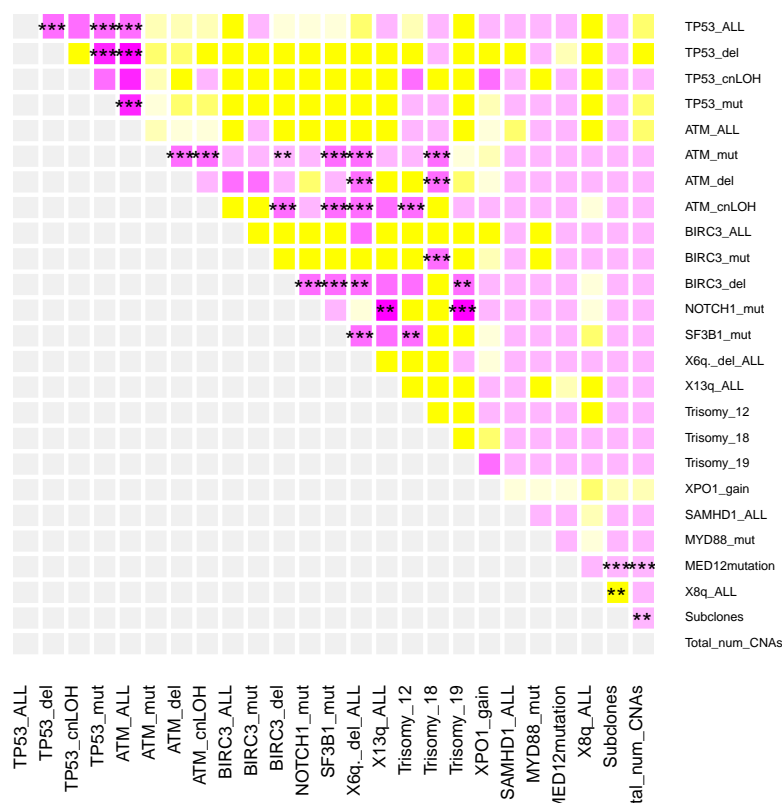
	variables	TP53_ALL	TP53_del	TP53-cnLOH	TP53_mut	ATM_ALL	ATM_mut	ATM_del	ATM-cnLOH	BIRC3_ALL	BIRC3_mut	BIRC3_del	NOTCH1_mut	SF3B1_mut	X6q_-delALL	X13q_-
p1	TP53_ALL															
p2	TP53_del			0.357	0	0	1	1	1	1	1	1	1	1	1	1
p3	TP53-cnLOH			1		0	1	1	1	1	1	1	1	1	1	1
p4	TP53_mut				1	0	1	1	1	1	1	1	1	1	1	1
p5	ATM_ALL					0.463	1	1	1	1	1	1	1	1	1	1
p6	ATM_mut					0	1	1	1	1	1	1	1	1	1	1
p7	ATM_del							0		1	0.301	0.003	1	0	0	1
p8	ATM-cnLOH								0.726	1	0.027	1	1	1	1	1
p9	BIRC3_ALL									1	1	0	1	0	0	0.55
p10	BIRC3_mut										1	0	1	1	0.078	1
p11	BIRC3_del											1	1	1	1	1
p12	NOTCH1_mut												0	0	0.43	1
p13	SF3B1_mut													1	0.004	0.00
p14	X6q_-delALL														1	0.00
p15	X13q_ALL															0.12
p16	Trisomy_12															1
p17	Trisomy_18															1
p18	Trisomy_19															1
p19	XPO1_gain															1
p20	SAMHD1_ALL															1
p21	MYD88_mut															1
p22	MED12mutation												0	0	0.004	0.00
p23	X8q_ALL													1	1	0.00
p24	Subclones														0.001	0.12
p25	Totalnum_CNAs															1

Odds ratios and p-values for association between genes are represented in this heat map. Note that blue is mutually exclusive, red is associated. Also, the colour key is not symmetrical, colours used:

- -3 -> oddsratio<0.1
- -2 -> oddsratio>=0.1 oddsratio < 0.2
- -1 -> oddsratio>=0.2 oddsratio < 0.4
- 0 -> oddsratio>=0.4 oddsratio < 0.6
- 1 -> oddsratio>=0.6 oddsratio < 0.8
- 2 -> oddsratio>=1 oddsratio < 3
- 3 -> oddsratio>=3 oddsratio < 10
- 4 -> oddsratio>=10 oddsratio < 15
- 5 -> oddsratio>=15 oddsratio < 20
- 6 -> oddsratio>20



Association for n=239



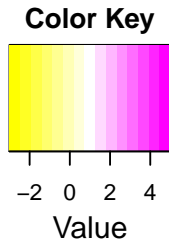
Model building - from here, only 209 data points will be used

Association on model data

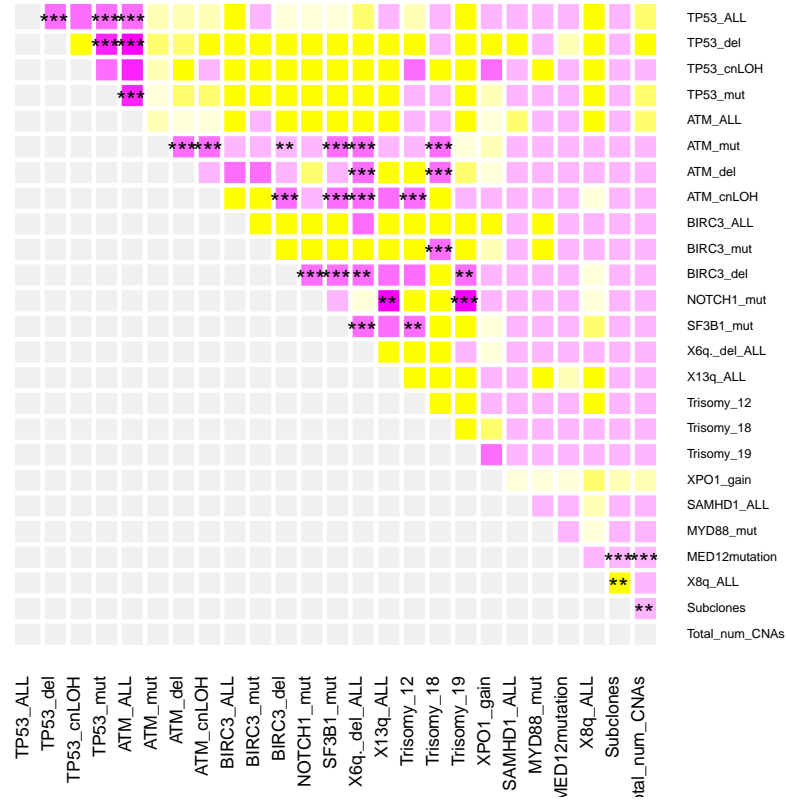
This was calculated to see if there are Co-linearities that have to be taken into account for the modelling. There are fewer associations than in the 239 data set, but as you can see from the chart, the associations don't change much.

Table 4: Corrected p-values for association between genetic lesions, n=209

p	variables	TP53-ALL	TP53-del	TP53.cnLOH	TP53.mut	ATM-ALL	ATM-mut	ATM-del	ATM.cnLOH	BIRC3-ALL	BIRC3.mut	BIRC3.del	NOTCH1-mut	SF3B1-mut	X6q-del-ALL	X13q-ALL
p1	TP53-ALL															
p2	TP53-del		0	0.357	0	0	1	1	1	1	1	1	1	1	1	1
p3	TP53.cnLOH			1	0	0	1	1	1	1	1	1	1	1	1	1
p4	TP53.mut				1	0.463	1	1	1	1	1	1	1	1	1	1
p5	ATM-ALL					0	1	1	1	1	1	1	1	1	1	1
p6	ATM-mut							1	1	1	1	1	1	1	1	1
p7	ATM-del							0	0	1	0.301	0.003	1	0	0	1
p8	ATM.cnLOH							0.726	0.726	1	0.027	1	1	1	0	1
p9	BIRC3-ALL									1	1	0	1	0	0	0.533
p10	BIRC3-mut										1	1	1	1	0.078	1
p11	BIRC3-del											1	1	1	1	1
p12	NOTCH1-mut												0	0	0.004	0.437
p13	SF3B1-mut													1	1	0.005
p14	X6q-del-ALL														1	0.124
p15	X13q-ALL															1
p16	Trisomy-12															
p17	Trisomy-18															
p18	Trisomy-19															
p19	XPO1-gain															
p20	SAMHD1-ALL															
p21	MYD88-mut															
p22	MED12mutation															
p23	X8q-ALL															
p24	Subclones															
p25	Total.num.CNAs															
p																



Model data, n=209



Multiple logistic regression models

The goal is to compare several different models and their quality, and eventually compare them to clinical parameters that are currently used.

Table 5: Multiple log regression, n=209

	Dependent variable:			
	MRD			
	genetic1	genetic2	genetic3	genetic4
TP53_ALL1	2.51*** (0.78)	2.67*** (0.78)		
TP53_mutdel1			17.77 (1,018.80)	17.87 (1,010.64)
ATM_bil	1.68*** (0.56)		1.69*** (0.55)	
ATM_del1				1.59*** (0.45)
BIRC3_mono1	-2.15* (1.27)		-1.66 (1.20)	-1.66 (1.17)
ATM_ALL1		0.99*** (0.33)		
Trisomy_121	-0.76 (0.48)	-0.82 (0.52)	-0.70 (0.47)	-0.59 (0.48)
NOTCH1_mut1	-0.61 (0.52)	-0.67 (0.53)	-0.56 (0.51)	-0.48 (0.52)
SAMHD1_ALL1	2.01** (0.89)	1.63** (0.83)		
SF3B1_mut1		-0.16 (0.44)		
SAMHD1_mut1			17.77 (1,426.72)	17.62 (1,378.88)
X13q_Ross1	-0.30 (0.36)	-0.20 (0.41)	-0.29 (0.36)	0.01 (0.36)
Constant	-0.17 (0.25)	-0.35 (0.35)	-0.16 (0.24)	-0.37 (0.26)
Observations	209	209	209	209
Log Likelihood	-121.23	-123.45	-116.96	-115.67
Akaike Inf. Crit.	258.46	262.89	249.92	247.33

Note: * p<0.1; ** p<0.05; *** p<0.01

Discussion of different models

Table 6: Multiple log regression, n=209

	<i>Dependent variable:</i>				
	genetic5	genetic6	MRD genetic7	vh mutation	Binet
TP53_mut1	17.77 (1,018.80)	17.74 (1,018.47)			
TP53_mutdel1			17.93 (1,016.65)		
ATM_b1	1.69*** (0.55)	1.68*** (0.56)	1.76*** (0.56)		
BIRC3_monol	-1.66 (1.20)	-1.66 (1.20)	-1.82 (1.18)		
Trisomy_121	-0.70 (0.47)	-0.69 (0.47)			
NOTCH1_mut1	-0.56 (0.51)	-0.56 (0.51)	-0.51 (0.52)		
SAMHD1_mut1	17.77 (1,426.72)	17.77 (1,428.10)	17.87 (1,415.25)		
X13q_Ross1	-0.29 (0.36)	-0.30 (0.37)	-0.06 (0.41)		
SF3B1_mut1			0.22 (0.42)		
Subclones		0.02 (0.25)	0.03 (0.25)		
vh_mutation_statusunmutated				1.15*** (0.31)	
BinetC					0.12 (0.29)
Constant	-0.16 (0.24)	-0.17 (0.26)	-0.42 (0.28)	-0.75*** (0.24)	-0.09 (0.17)
Observations	209	209	209	181	209
Log Likelihood	-116.96	-116.96	-117.94	-118.14	-144.73
Akaike Inf. Crit.	249.92	251.91	253.87	240.28	293.46

Note:

*p<0.1; **p<0.05; ***p<0.01