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
p	TP53_ALL	0.00004	***	0.001	***	105	19	2	209	Fisher's Exact Test
p	TP53_mut	0.00001	***	0.0003	***	107	15	0	209	Fisher's Exact Test
p	TP53_bi	0.009	**	0.128	n.s.	106	9	1	209	Fisher's Exact Test
p	ATM_ALL	0.002	**	0.033	*	83	44	24	209	Fisher's Exact Test
p	ATM_del	0.0005	***	0.009	**	98	28	9	209	Fisher's Exact Test
p	BIRC3_ALL	0.094	trend	0.850	n.s.	94	22	13	209	Fisher's Exact Test
p	BIRC3_del	0.002	**	0.031	*	101	21	6	209	Fisher's Exact Test
p	ATM_bi	0.002	**	0.033	*	102	19	5	209	Fisher's Exact Test
p	BIRC3_bi	0.360	n.s.	1	n.s.	106	3	1	209	Fisher's Exact Test
p	ATM_mono	0.836	n.s.	1	n.s.	93	12	14	209	Fisher's Exact Test
p	BIRC3_mono	0.066	trend	0.723	n.s.	100	1	7	209	Fisher's Exact Test
p	NOTCH1_mut	0.069	trend	0.723	n.s.	88	9	19	209	Fisher's Exact Test
p	SF3B1_mut	0.415	n.s.	1	n.s.	85	26	22	209	Fisher's Exact Test
p	Trisomy_12	0.002	**	0.036	*	82	8	25	209	Fisher's Exact Test
p	SAMHD1_ALL	0.054	trend	0.657	n.s.	105	8	2	209	Fisher's Exact Test
p	Subclones	0.050	trend	0.657	n.s.					Wilcoxon Test
p	Total_num_CNAs	0.483	n.s.	1	n.s.					Wilcoxon Test
p	Binet	0.770	n.s.	1	n.s.	72	36	35	209	Fisher's Exact Test
page_at_randomisation		0.100	trend	0.850	n.s.					Wilcoxon Test
p	patient_gender	0.443	n.s.	1	n.s.	33	76	74	209	Fisher's Exact Test
p	vh_mutation_status	0.0003	***	0.006	**	55	60	40	181	Fisher's Exact Test
p	WBC	0.013	*	0.179	n.s.					Wilcoxon Test
p	cd38	0.707	n.s.	1	n.s.	45	40	59	147	Fisher's Exact Test

Associations

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

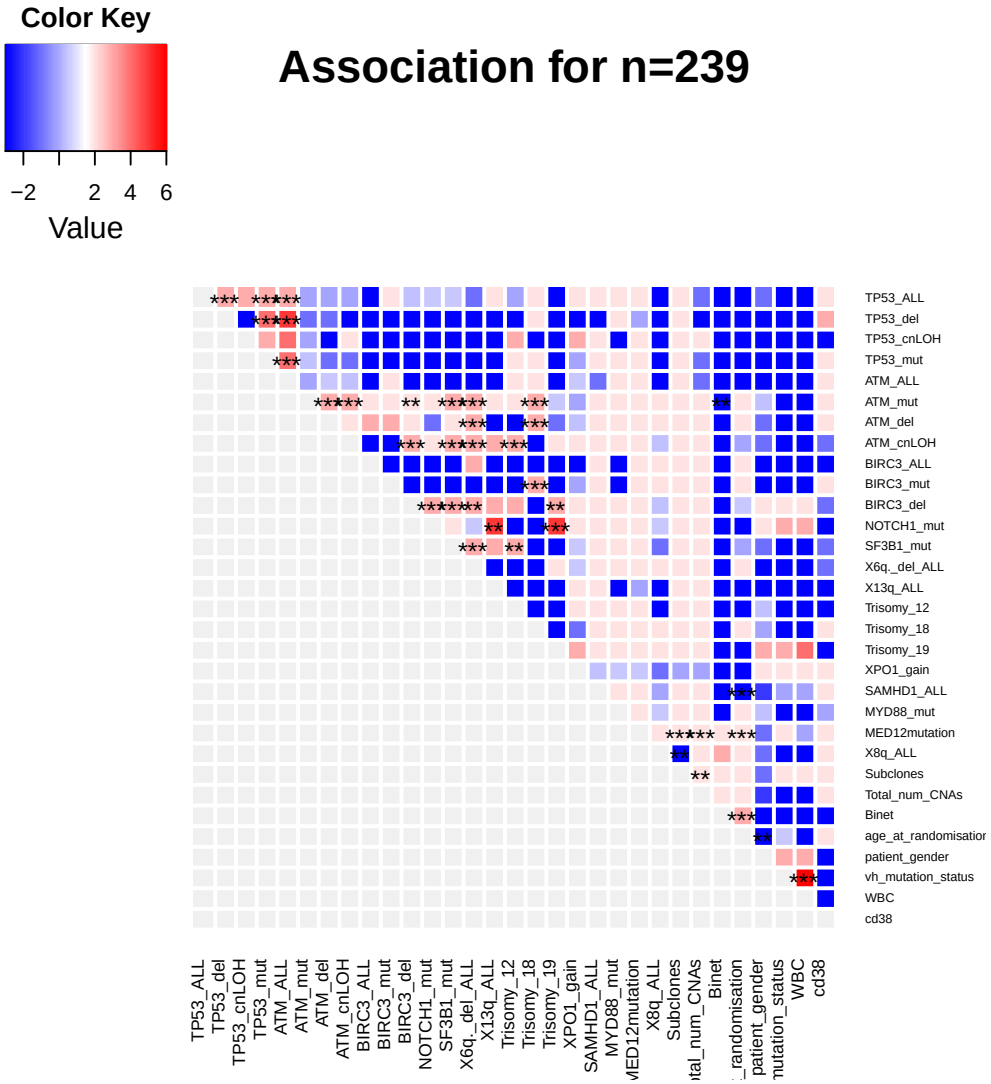
p	variables	TP53_ALL	TP53_del	TP53_cnLOH	TP53_mut	ATM_ALL	ATM_mut	ATM_del	ATM_cnLOH	BIRC3_ALL	BIRC3_mut	BIRC3_del	NOTCH1_mut	SF3B1_mut	X6q._del_ALL	X
p 1	TP53_ALL		0	0.001	0	0	0.510	0.571	0.498	1	0.411	0.343	1	0.593	0.386	
p 2	TP53_del			1	0	0	0.274	0.530	0.429	1	1	0.422	1	0.642	0.634	
p 3	TP53_cnLOH				0.005	0.002	1	0.632	0.505	1	1	1	1	1	1	
p 4	TP53_mut					0	0.173	0.186	0.275	1	0.631	0.087	0.642	0.189	0.181	
p 5	ATM_ALL						0.642	0.595	0.527	1	0.505	0.183	1	0.429	0.416	
p 6	ATM_mut							0	0	0.031	0.001	0	0.373	0	0	
p 7	ATM_del								0.003	0.011	0	0.111	0.197	0.017	0	
p 8	ATM_cnLOH									1	0.283	0	0.018	0	0	
p 9	BIRC3_ALL										1	1	1	1	0	
p10	BIRC3_mut											0.277	1	0.413	0.650	
p11	BIRC3_del												0	0	0	
p12	NOTCH1_mut													0.042	1	
p13	SF3B1_mut														0	
p14	X6q._del_ALL															
p15	X13q_ALL															
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															
p26	Binet															
p27	age_at_randomisation															
p28	patient_gender															
p29	vh_mutation_status															
p30	WBC															
p31	cd38															

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._del_ALL	X
p 1	TP53_ALL		0	0.558	0	0	1	1	1	1	1	1	1	1	1	
p 2	TP53_del			1	0	0	1	1	1	1	1	1	1	1	1	
p 3	TP53_cnLOH				1	0.727	1	1	1	1	1	1	1	1	1	
p 4	TP53_mut					0	1	1	1	1	1	1	1	1	1	
p 5	ATM_ALL						1	1	1	1	1	1	1	1	1	
p 6	ATM_mut							0	0	1	0.470	0.005	1	0	0	
p 7	ATM_del								1	1	0.042	1	1	1	0	
p 8	ATM_cnLOH									1	1	0	1	0	0	
p 9	BIRC3_ALL										1	1	1	1	0.122	
p10	BIRC3_mut											1	1	1	1	
p11	BIRC3_del												0	0	0.007	
p12	NOTCH1_mut													1	1	
p13	SF3B1_mut														0.001	
p14	X6q._del_ALL															
p15	X13q_ALL															
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															
p26	Binet															
p27	age_at_randomisation															
p28	patient_gender															
p29	vh_mutation_status															
p30	WBC															
p31	cd38															

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



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

Logistic regression model

Simple logistic regression models

For these models, I used the variables that turned out significant in the univariate analysis (model 1-4 in table 5). This is a commonly used procedure, but it can mean that I selected variables that are highly colinear (or co-occuring), TP53 variables for example.

Summarized Model

For these models, I summarized the data even more:

- all trisomies are grouped together
- for each lesion, I used the broadest variable

Table 4: Multiple log regression, n=209

	Dependent variable:	
	MRD	
	genetic 1	genetic2
TP53_ALL1	2.51^{***} (0.78)	2.67^{***} (0.78)
ATM_bi1	1.68^{***} (0.56)	
BIRC3_mono1	-2.15^{*} (1.27)	
ATM_ALL1		0.99^{***} (0.33)
Trisomy_121	−0.76 (0.48)	−0.82 (0.52)
NOTCH1_mut1	−0.61 (0.52)	−0.67 (0.53)
SAMHD1_ALL1	2.01^{**} (0.89)	1.63^{**} (0.83)
SF3B1_mut1		−0.16 (0.44)
X13q_Rossi1	−0.30 (0.36)	−0.20 (0.41)
Constant	−0.17 (0.25)	−0.35 (0.35)
Observations	209	209
Log Likelihood	−121.23	−123.45
Akaike Inf. Crit.	258.46	262.89
Note:	*p<0.1; **p<0.05; ***p<0.01	