Fanconi anemia and homologous recombination gene variants are associated with functional DNA repair defects in vitro and poor outcome in patients with advanced head and neck squamous cell carcinoma

Verhagen, C.V.M.; Vossen, D.M.; Borgmann, K.; Hageman, F.; Grénman, R.; Verwijs-Jansen, M.; Mout, L.; Kluin, R.J.C.; Nieuwland, M.; Severson, T.M. ; Velds, A.; Kerkhoven, R.; O'Connor, M.J.; van der Heijden, M.; van Velthuysen, M.-L.; Verheij, M.; Wreesmann, V.B.; Wessels, L.F.A.; van den Brekel, M.W.M.; Vens, C.

DOI
10.18632/oncotarget.24797

Publication date
2018

Document Version
Other version

Published in
Oncotarget

Supplementary Table 5A: References and characteristics of selected canonical FA/HR gene set variants in the tumor samples of the patients in the study

Pts	Gene	Protein change	SNP ID	cosmic70	MAF 1000G	CADD	REVEL	SIFT	PolyPhen2	ClinVar	Comments to potential functional effects	REF PMID
1	PALB2	L337S	rs45494092		0,0249	8.918	0.041	Deleterious	B	Conflicting interpretations	Possibly enriched in familial cutaneous malignant melanoma. Similar frequency in breast cancer than controls.	24949998 21618343 26283626
	FANCC	V60I	rs138629441			0.185	0.101	T	B	Likely benign (Fanconi Anemia)	Unlikely to affect function	14695169
	FANCG	R513Q	rs17885240		0,0129	15.01	0.016	T	B	Likely benign (Fanconi Anemia)	Increased frequency in children with AML	16643430
2	PALB2	T1099R	rs142132127	ID=COSM1666745		16	0.214	Deleterious	Damaging	Uncertain significance	Semiconservative AS substitution in conserved 5th WD repeat, region of BRCA2, RAD51 and POLH interaction. Possible enrichment in individuals with breast or ovarian cancer.	25186627 26315354
3	PALB2	L337S	rs45494092		0,0249	8.918	0.041	Deleterious	B	*as above*	*see above*	*see above*
4	FANCG	R513Q	rs17885240		0,0129	15.01	0.016	T	B	*as above*	*see above*	*see above*
5	FANCG	R513Q	rs17885240		0,0129	15.01	0.016	T	B	*as above*	*see above*	*see above*
6	FANCM	K953N	rs142864437			14.93	0.085	Deleterious	Damaging	Uncertain significance	No reports found	
	FANCA	A554V				19.95	0.636	T	Damaging		No reports found	
7	FANCM	T77A	rs61746895		0,0129	2.724	0.041	T	B	Likely benign (Fanconi Anemia)	Neighboring MPH1 (ERCC4-related helicase) region	
8	FANCF	P320L	rs45451294		0,0119	16.83	0.096	T	Possibly Damaging	Benign (Fanconi Anemia)	No reports found	
	FANCF	R38H				23.2	0.14	Deleterious	Damaging		No reports found	
9	FANCF	P320L	rs45451294		0,0119	16.83	0.096	T	Possibly Damaging	*as above*	*see above*	*see above*
10	FANCD2	N545S	rs145522204		0,0089	0.887	0.053	T	B	Benign	No reports found	
11	FANCD2	R997Q				15.1	0.091	T	B		No reports found	
12	FANCC	H256R				16.51	0.058	T	B		Reported in one individual in controls in pancreatic cancer study	15695377
13	RAD51C	G264S	rs147241704			23	0.202		B	Uncertain significance	Non-conservative amino acid substitution in conserved region (ATPase domain) LOVD: hypomorph feature: partial complementation in cells, normal Rad51 foci; Increased frequency in breast / ovarian Moderate penetrance suggestion in ovarian cancer	20400964 21990120

14	RAD51B	K243R	rs34594234		0,0089	25.4	0.186	T	Damaging			
15	BRCA1	R841W	rs1800709	ID=COSM1246204	0,005	5.12	0.355	Deleterious	Possibly Damaging	Benign (Hereditary Can)	Referenced in LOVD; Predicted to affect function in evolutionary conservation analysis Likely pathogenic through bayesian analysis considering breast cancer family frequencies neighboring 840S is phosphorylation site	22753008 21520273 18415037 8968716

Abbreviations and listing as in Supplementary Table 4.