SUPPLEMENTAL MATERIAL

TP53 Mutational Spectrum in Endometrioid and Serous Endometrial Cancers

Schultheis et al.

Supplemental Tables 1-5

Supplemental Figure 1

SUPPLEMENTAL TABLES

Supplemental Table 1. Endometrial cancers harboring multiple *TP53* mutations.

ID	Histology	FIGO grade	Integrative genomic subtype	*TP53* mutation	*TP53* hotspot mutation
TCGA-BS-A0UV	Endometrioid	Grade 3	POLE	R158C, R213*	0
TCGA-B5-A11N	Endometrioid	Grade 1	POLE	R209I, T256fs	0
TCGA-D1-A16Y	Endometrioid	Grade 1	POLE	R213Q, S241P	0
TCGA-AP-A059	Endometrioid	Grade 3	POLE	P64T, S240G, R273C	1

POLE, POLE (ultramutated) integrative genomic subtype. Hotspot *TP53* mutations include R175, G245, R248, R249, R273 and R282.

Supplemental Table 2. *TP53* status in endometrioid endometrial carcinomas according to FIGO grade.

		Endometrioid endometrial carcinomas (n=186)		p-value*
		Wild-type *TP53* (n)	Mutant *TP53* (n)	
FIGO grade	Grade 1	68	2	<0.0001
	Grade 2	72	8	
	Grade 3	46	17	

*, Chi-squared p-value; n=number of cases

Supplemental Table 3. *TP53* status of endometrial cancers of copy-number high integrative genomic subtype and co-occurrence with somatic mutations in genes frequently altered in endometrial cancers.

		CN-high endometrioid (n=16)	**CN-high serous (n=41)**	**p-value***
TP53 mutation		15 (94%)	37 (90%)	1.0
Type of *TP53* mutation	Frameshift	2	4	1.0
	Missense	12	29	
	Nonsense	1	3	
	Splice	0	1	
Hotspot *TP53* mutation	No	12	24	0.2096
	Yes	3	17	
ARID1A gene status	Wild-type	16	38	0.5516
	Mutant	0	3	
FBXW7 gene status	Wild-type	16	28	0.0116
	Mutant	0	13	
PPP2R1A gene status	Wild-type	15	30	0.1477
	Mutant	1	11	
PTEN gene status	Wild-type	11	40	0.0052
	Mutant	5	1	
		CN-high *TP53*-mutant endometrioid (n=15)	**CN-high *TP53*-mutant serous (n=37)**	**p-value***
ARID1A gene status	Wild-type	15	34	0.5480
	Mutant	0	3	
FBXW7 gene status	Wild-type	15	36	0.0518
	Mutant	0	11	
PPP2R1A gene status	Wild-type	14	27	0.1447
	Mutant	1	10	
PTEN gene status	Wild-type	10	36	0.0057
	Mutant	5	1	

*, Fisher's exact test p-value

CN-high, copy-number high (serous-like) integrative genomic subtype. Hotspot *TP53* mutations include R175, G245, R248, R249, R273 and R282.

Supplemental Table 4. Prevalence of somatic mutations in genes frequently altered in *TP53* wild-type and *TP53*-mutant endometrioid and serous endometrial carcinomas.

	All endometrioid (n=186)	**All serous (n=42)**	**p-value***
ARID1A gene status	73/186 (39%)	4/42 (10%)	0.0001
PTEN gene status	146/186 (78%)	1/42 (2%)	<0.0001
FBXW7 gene status	23/186 (12%)	14/42 (33%)	0.00206
PPP2R1A gene status	13/186 (7%)	11/42 (26%)	0.00098
	***TP53* wild-type endometrioid (n=159)**	***TP53* wild-type serous (n=5)**	**p-value***
ARID1A gene status	69/159 (43%)	1/5 (20%)	0.3944
PTEN gene status	129/159 (81%)	0/5 (0%)	0.0003
FBXW7 gene status	20/159 (13%)	3/5 (60%)	0.0202
PPP2R1A gene status	11/159 (7%)	1/5 (20%)	0.3194
	***TP53*-mutant endometrioid (n=27)**	***TP53*-mutant serous (n=37)**	**p-value***
ARID1A gene status	4/27 (15%)	3/37 (8%)	0.4427
PTEN gene status	17/27 (63%)	1/37 (3%)	0.0001
FBXW7 gene status	3/27 (11%)	11/37 (30%)	0.1247
PPP2R1A gene status	2/27 (7%)	10/37 (27%)	0.0578
	FIGO grade 3 *TP53*-mutant endometrioid (n=17)	***TP53*-mutant serous (n=37)**	**p-value***
ARID1A gene status	4/17 (24%)	3/37 (8%)	0.1885
PTEN gene status	10/17 (59%)	1/37 (3%)	0.0001
FBXW7 gene status	1/17 (6%)	11/37 (30%)	0.0778
PPP2R1A gene status	1/17 (6%)	10/37 (27%)	0.1427
	CN-high FIGO grade 3 *TP53*-mutant endometrioid (n=9)	**CN-high *TP53*-mutant serous (n=37)**	**p-value***
ARID1A gene status	0/9 (0%)	3/37 (8%)	1.0
PTEN gene status	2/9 (22%)	1/37 (3%)	0.0933
FBXW7 gene status	0/9 (0%)	11/37 (30%)	0.0890
PPP2R1A gene status	0/9 (0%)	10/37 (27%)	0.1722

*, Fisher's exact test p-value

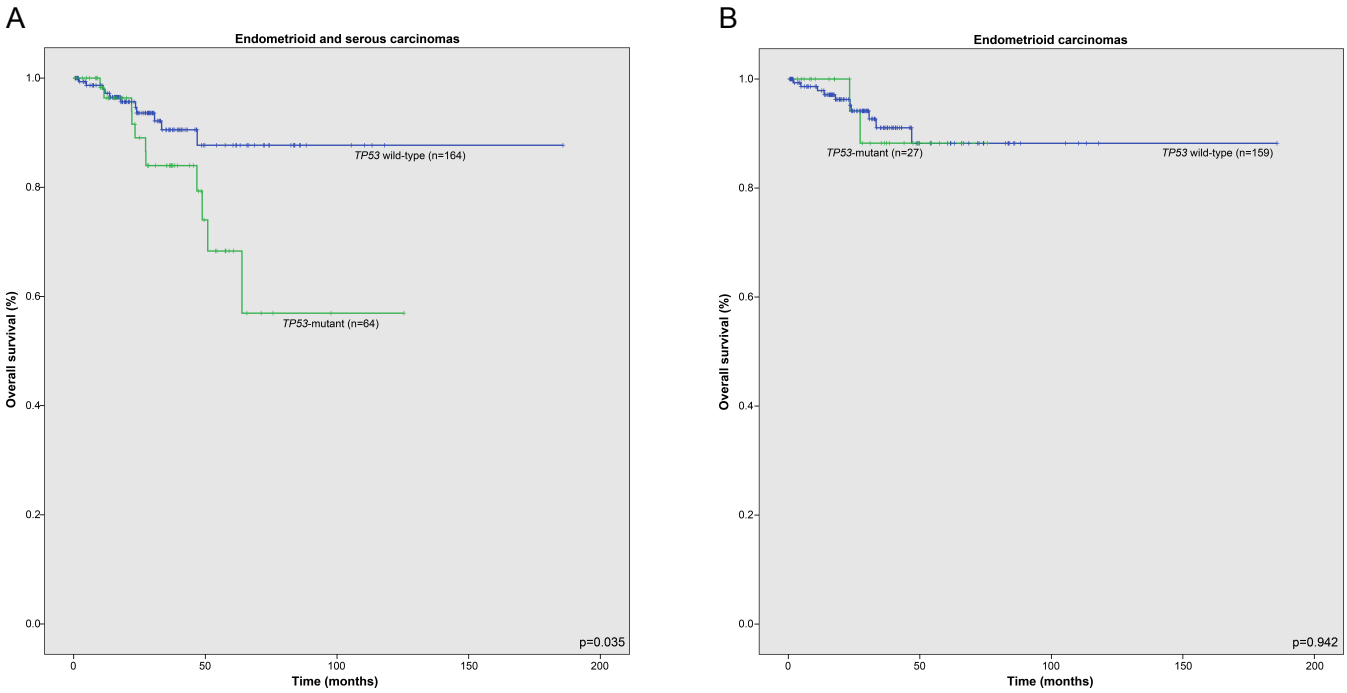
CN-high, copy-number high (serous-like) integrative genomic subtype.

Supplemental Table 5. Clinico-pathologic characteristics of and genomic alterations in *TP53* wild-type serous endometrial carcinomas.

TCGA ID	FIGO stage	MSI status	Integrative genomic subtype	Non-synonymous mutations (n)*	Copy number altered genes (n)*	Genes mutated preferentially in SECs**	Genes mutated preferentially in EECs**
TCGA-B5-A1MY	III	MSS	CN-high	43	238		
TCGA-AX-A1C7	I	MSS	CN-high	40	303	*FBXW7*	
TCGA-B5-A0K8	I	MSS	CN-high	41	1133	*PPP2R1A*	
TCGA-D1-A0ZP	IV	MSI-L	CN-high	30	1077	*FBXW7*, *CHD4*, *PIK3CA*	*PIK3CA*
TCGA-D1-A15X	I	MSI-L	CN-low	1324	5	*FBXW7*, *PIK3CA*	*KRAS*, *ARID1A*, *PIK3CA*, *FGFR2*

CN-high, copy-number high (serous-like) integrative genomic subtype; CN-low, copy-number low (serous-like) integrative genomic subtype; EEC, endometrioid endometrial cancer; MSI, microsatellite instability; MSI-L, low level microsatellite instability; MSS, microsatellite stable; SEC, serous endometrial cancer. *information retrieved from www.cBioPortal.org (April 2015); ***according to the significantly mutated genes reported in The Cancer Genome Atlas study, Nature 2013.

Supplemental Figure 1



Supplemental Fig. 1. Kaplan-Meier overall survival curves for endometrial carcinomas. (A) Kaplan-Meier overall survival curve for all 228 endometrioid and serous endometrial carcinomas included in this study stratified by *TP53* mutation status. (B) Kaplan-Meier overall survival curve for the 186 endometrioid endometrial carcinomas included in this study stratified by *TP53* mutation status.