

SUPPLEMENTARY MATERIALS

Recurrent *MED12* exon 2 mutations in benign breast fibroepithelial lesions in adolescents and young adults

Pareja et al.

Supplementary Table S1: Primers used for Sanger Sequencing.

Supplementary Table S2: *MED12* exon 2 mutations identified in 29 benign breast fibroepithelial lesions in adolescents and young adults, and their predicted pathogenicity.

Supplementary Table S3: Clinicopathological features and *MED12* and *TERT* mutational status of fibroadenomas in adolescents and young adults.

Supplementary Table S4: Clinicopathological features of fibroadenomas in adolescents and young adults according to *MED12* mutational status.

Supplementary Table S5: Clinicopathological features and *MED12* and *TERT* mutational status of benign phyllodes tumors in adolescents and young adults.

Supplementary Table S6: Clinicopathological features of benign phyllodes tumors in adolescents and young adults, according to *MED12* mutational status.

Supplementary Table S1: Primers used for Sanger Sequencing.

Gene	Forward	Reverse
<i>MED12</i> exon 2 <i>TERT</i> promoter	TGTTCTACACGGAACCCTCCTC CCAGGGCTTCCCACGTGC	CTGGGCAAATGCCAATGAGAT ACTGGGGACCCGGGCACC

Supplementary Table S2: *MED12* exon 2 mutations identified in 29 benign breast fibroepithelial lesions in adolescents and young adults, and their predicted pathogenicity.

Sample ID	Age (years)	Diagnosis	Tumor size (cm)	<i>MED12</i> Amino Acid Change	Effect	<i>MED12</i> cDNA change	Start Position	End Position	MutationTaster	Provean	Polyphen-2	CADD	In COSMIC*	COSMIC* Mutation ID	<i>TERT</i> status
JF1	19	BePT	0.7	p.G44D	Missense	c.131G>A	70339254	70339254	disease causing	deleterious	probably damaging	deleterious	Yes	COSM131596	WT
JF2	21	FA	2.6	WT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	WT
JF3	17	FA	6	p.G44D	Missense	c.131G>A	70339254	70339254	disease causing	deleterious	probably damaging	deleterious	Yes	COSM131596	WT
JF4	17	FA	1.2	WT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	WT
JF5	18	BePT	1	p.G44_G53del	In-frame indel	c.132_158del	70339255	70339281	NA	deleterious	NA	deleterious	Yes	COSM5991498	WT
JF6	18	FA	1.3	p.G44S	Missense	c.130G>A	70339253	70339253	disease causing	deleterious	probably damaging	deleterious	Yes	COSM131594	WT
JF7	19	BePT	2.2	p.L39_G53delinsW	In-frame indel	c.116_157del	70339239	70339280	NA	deleterious	NA	deleterious	No	NA	WT
JF8	14	FA	1.2	WT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	WT
JF9	17	FA	3.6	p.G44D	Missense	c.131 G>A	70339254	70339254	disease causing	deleterious	probably damaging	deleterious	Yes	COSM131596	WT
JF10	15	BePT	4.4	p.L39_A50delinsF	In-frame indel	c.117_149del	70339240	70339272	NA	deleterious	NA	deleterious	Yes	COSM5991544	WT
JF11	20	FA	0.9	p.L39_V51del	In-frame indel	c.114_152del	70339237	70339275	NA	deleterious	NA	deleterious	No	NA	WT
JF12	22	FA	2.8	p.L39_D54del	In-frame indel	c.115_162del	70339238	70339285	NA	deleterious	NA	deleterious	Yes	COSM5010451	WT
JF14	23	FA	4.9	p.G44D	Missense	c.131G>A	70339254	70339254	disease causing	deleterious	probably damaging	deleterious	Yes	COSM131596	WT
JF15	19	FA	2.2	WT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	WT
JF16	13	FA	10.5	WT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	WT
JF17	25	FA	1.5	p.A38_K42del	In-frame indel	c.111_125del	70339234	70339248	NA	deleterious	NA	deleterious	No	NA	WT
JF18	20	FA	1	p.N40_P49delinsT	In-frame indel	c.119_145del	70339242	70339268	NA	deleterious	NA	deleterious	Yes	COSM5415276	WT
JF19	25	BePT	0.9	p.P49_E55del	In-frame indel	c.146_166del	70339269	70339289	NA	deleterious	NA	deleterious	Yes	COSM1235335	WT
JF20	23	FA	2.5	p.Q43_D54delinsH	In-frame indel	c.129_161del	70339252	70339284	NA	deleterious	NA	deleterious	No	NA	WT
JF21	25	FA	3.5	p.Q48_H56del	In-frame indel	c.142_168del	70339265	70339291	NA	deleterious	NA	deleterious	Yes	COSM5715352	WT
JF24	21	BePT	2.4	p.G44C	Missense	c.130G>T	70339253	70339253	disease causing	deleterious	probably damaging	deleterious	Yes	COSM131593	WT
JF25	26	FA	5.8	WT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	WT
JF26	17	FA	2.2	p.G44R	Missense	c.130G>C	70339253	70339253	disease causing	deleterious	probably damaging	deleterious	Yes	COSM131592	WT
JF27	24	FA	1	p.X34_splice	Splice-site	c.100-13_100-1del	70339210	70339222	NA	N/A	NA	deleterious	No	NA	WT
JF28	18	BePT	1.3	WT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	WT
JF29	18	FA	4	p.V41_S52del	In-frame indel	c.121_156del	70339244	70339279	NA	deleterious	NA	deleterious	Yes	COSM5415266	WT
JF31	18	FA	3.8	WT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	WT
JF32	16	FA	4	WT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	WT
JF34	18	BePT	1.4	p.G44_P49del	In-frame indel	c.132_146del	70339255	70339269	NA	deleterious	NA	deleterious	Yes	COSM6006399	WT

BePT, benign phyllodes tumor; FA, fibroadenoma; NA, not applicable; WT, wild type

*COSMIC V84 was used

Supplementary Table S3: Clinicopathological features and *MED12* and *TERT* mutational status of fibroadenomas in adolescents and young adults.

Sample ID	Age (years)	Laterality	Size (cm)	Growth pattern	<i>MED12</i> mutation	<i>TERT</i> status
JF2	21	Right	2.6	Pericanalicular	WT	WT
JF3	17	Left	6	Intracanalicular	p.G44D	WT
JF4	17	Right	1.2	Pericanalicular	WT	WT
JF6	18	Left	1.3	Mixed	p.G44S	WT
JF8	14	Left	1.2	Pericanalicular	WT	WT
JF9	17	Right	3.6	Intracanalicular	p.G44D	WT
JF11	20	Right	0.9	Intracanalicular	p.L39_V51del	WT
JF12	22	Left	2.8	Intracanalicular	p.L39_D54del	WT
JF14	23	Right	4.9	Intracanalicular	p.G44D	WT
JF15	19	Left	2.2	Pericanalicular	WT	WT
JF16	13	Right	10.5	Pericanalicular	WT	WT
JF17	25	Right	1.5	Intracanalicular	p.A38_K42del	WT
JF18	20	Left	1	Intracanalicular	p.N40_P49delinsT	WT
JF20	23	Left	2.5	Intracanalicular	p.Q43_D54delinsH	WT
JF21	25	Right	3.5	Intracanalicular	p.Q48_H56del	WT
JF25	26	Right	5.8	Pericanalicular	WT	WT
JF26	17	Left	2.2	Pericanalicular	p.G44R	WT
JF27	24	Right	1	Intracanalicular	p.X34_splice	WT
JF29	18	Left	4	Intracanalicular	p.V41_S52del	WT
JF31	18	Left	3.8	Pericanalicular	WT	WT
JF32	16	Left	4	Mixed	WT	WT

WT, wild type

Supplementary Table S4: Clinicopathological features of fibroadenomas in adolescents and young adults according to *MED12* mutational status.

Clinicopathologic feature		<i>MED12</i> ^{MUT} FAs (n=13)	<i>MED12</i> ^{WT} FAs (n=8)	<i>p</i> value
Age (years)	Median (range)	20 (17-25)	18 (13-26)	0.106 ^a
Size (cm)	Median (range)	2.5 (0.9-6)	3.2 (1.2-10.5)	0.252 ^a
Growth pattern	Intracanalicular	11 (84.6%)	0 (0%)	<0.001 ^b
	Pericanalicular	1 (7.7%)	1 (12.5%)	
	Mixed	1 (7.7%)	7 (87.5%)	

FA, fibroadenoma; MUT, mutant; WT, wild-type; ^aStudent's t test; ^bFisher's exact test

Supplementary Table S5: Clinicopathologic features and *MED12* and *TERT* mutational status of benign phyllodes tumors in adolescents and young adults.

Sample ID	Age (years)	Laterality	Size (cm)	Tumor border	Stromal cellularity	Stromal atypia	Stromal overgrowth	Mitoses/ 10 HPF	<i>MED12</i> mutation	<i>TERT</i> status
JF1	19	Left	0.7	Well defined	Low	Mild	Absent	1	p.G44D	WT
JF5	18	Left	1	Well defined	Low to intermediate	Mild	Absent	2	p.F45_G53del	WT
JF7	19	Left	2.2	Well defined	Low	Mild	Absent	1	p.L39_G53delinsW	WT
JF10	15	Right	4.4	Well defined	Low	Mild	Absent	0	p.L39_A50delinsF	WT
JF19	25	Right	0.9	Well defined	Low	Mild	Absent	0	p.P49_E55del	WT
JF24	21	Right	2.4	Well defined	Low to intermediate	Mild	Absent	1	p.G44C	WT
JF28	18	Right	1.3	Well defined	Low	Mild	Absent	1	WT	WT
JF34	18	Right	1.4	Well defined	Low to intermediate	Mild	Absent	1	p.F45_P49del	WT

HPF, high power fields; WT, wild type

Supplementary Table S6: Clinicopathologic features of benign phyllodes tumors in adolescents and young adults, according to *MED12* mutational status.

Clinicopathologic feature		<i>MED12</i> ^{MUT} Ben PTs (n=7)	<i>MED12</i> ^{WT} Ben PTs (n=1)	p value
Age (years)	Median (range)	19 (15-25)	18 (-)	-
Size (cm)	Median (range)	1.4 (0.7-4.4)	1.3 (-)	-
Tumor border	Well defined	7 (100%)	1 (100%)	-
Stromal cellularity	Low	4 (57.1%)	1 (100%)	1.000 ^a
	Low to intermediate	3 (42.9%)	0 (0%)	
Stromal atypia	Mild	7 (100%)	1 (100%)	-
Mitoses/10 HPF	0	2 (28.6%)	0 (0%)	1.000 ^a
	1	4 (57.1%)	1 (100%)	
	2	1 (14.3%)	0 (0%)	
Stromal overgrowth	Absent	7 (100%)	1 (100%)	-

^aFisher's exact test; HPF, high power field; MUT, mutated, PT, phyllodes tumor; WT, wild-type