

Let-7 miRNA's Expression Profile and Its Potential Prognostic Role in Uterine Leiomyosarcoma

Bruna Cristine de Almeida¹, Laura Gonzalez dos Anjos¹, Miyuki Uno², Isabela Werneck da Cunha^{3,4,5}, Fernando Augusto Soares^{3,4,5}, Glauco Baiocchi⁶, Edmund Chada Baracat¹ and Katia Candido Carvalho^{1,*}

- ¹ Laboratório de Ginecologia Estrutural e Molecular (LIM 58), Disciplina de Ginecologia, Departamento de Obstetria e Ginecologia, Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, HCFMUSP, SP, BR Av. Dr Arnaldo 455, sala 4121, Cerqueira Cesar, São Paulo 05403-010, SP - Brazil; bruc_10@hotmail.com (B.C.A.); lauragonzalezanjost@gmail.com (L.G.d.A.); edmund.baracat@hc.fm.usp.br (E.C.B.)
- ² Centro de Investigação Translacional em Oncologia (LIM 24), Instituto do Câncer do Estado de São Paulo (CTO/ICESP) Av Dr Arnaldo 251 sala 23 8 andar; miyuki.uno@hc.fm.usp.br
- ³ Department of Pathology, Rede D'OR-São Luiz, Rua das Perobas, 344-Jabaquara, São Paulo 04321-120, Brazil
- ⁴ Hospital A C Camargo Cancer Center, SP, BR R. Tamandaré, 753 Liberdade, São Paulo 05403-010, Brazil; fsoares@me.com (F.A.S.); iwerneck0210@gmail.com (I.W.d.C.)
- ⁵ National Institute for Science and Technology in Oncogenomics and Therapeutic Innovation, SP, BR R. Tamandaré, 753 Liberdade, São Paulo 05403-010, Brazil
- ⁶ Department of Gynecology Oncology, A.C.Camargo Cancer Center, Rua Prof Antonio Prudente 211, São Paulo, Brazil; glaucobaiocchi@accamargo.org.br
- * Correspondence: carvalhokc@gmail.com; Tel.: +55-011-3061-7486

Table S1. Analysis of clinical and pathological features of patients treated with adjuvant therapy and untreated.

Variables	Adjuvant Therapy (n = 19)	No Adjuvant Therapy (n = 15)	p
Clinical FIGO stage			0.1907 ^a
1	5 (26%)	8 (53%)	
2	2 (11%)	3 (20%)	
3	5 (26%)	1 (7%)	
4	7 (37%)	3 (20%)	
Relapse			0.9135 ^b
No	6 (32%)	5 (33%)	
Yes	13 (68%)	10 (67%)	
Mitotic count (mitoses/10 high-power fields)			0.2421 ^b
≤10	0 (0%)	3 (%)	
≥10	8 (%)	9 (%)	
Metastasis			0.8622 ^a
No	1 (5%)	1 (7%)	
Local	6 (32%)	4 (27%)	
Distant	11 (58%)	8 (53%)	
Local e distant	1 (5%)	2 (13%)	
Menopause*			0.6980 ^b
Yes	5 (29%)	3 (21%)	
No	12 (71%)	11 (79%)	

* Patients treated with adjuvant therapy n = 17 and non-treated with adjuvant therapy n = 14; ^a Chi-square; ^b Fisher exact. FIGO, International Federation of Gynecology and Obstetrics.

Table S2. Patients ages analysis according to the miRNAs expression profile.

Age (years) n = 34	Downregulated Mean $\pm$ SD (min – max)	Upregulated Mean $\pm$ SD (min – max)	<i>p</i> *
<i>let-7a</i>	56.35 $\pm$ 18.24 (31 – 91)	52.82 $\pm$ 13.18 (27 – 75)	0.4641
<i>let-7b</i>	59.35 $\pm$ 16.83 (31 – 91)	49.82 $\pm$ 13.48 (27 – 75)	0.1048
<i>let-7c</i>	59.12 $\pm$ 15.69 (33 – 91)	50.06 $\pm$ 14.94 (27 – 84)	0.1335
<i>let-7d</i>	61.47 $\pm$ 16.34 (31 – 91)	47.71 $\pm$ 12.06 (27 – 72)	0.0158
<i>let-7e</i>	60.94 $\pm$ 16.33 (33 – 91)	48.24 $\pm$ 12.67 (27 – 72)	0.0191
<i>let-7f</i>	61.63 $\pm$ 15.37 (40 – 91)	48.33 $\pm$ 13.66 (27 – 78)	0.0160
<i>let-7g</i>	57.47 $\pm$ 17.49 (31 – 91)	51.71 $\pm$ 13.77 (27 – 78)	0.2242
<i>let-7i</i>	56.24 $\pm$ 16.10 (31 – 91)	52.94 $\pm$ 15.76 (27 – 84)	0.5349

* *t* teste.**Table S3.** Comparison between clinical and pathological features and the *let-7a* expression.

Variables	n (%)	<i>let-7a</i>		<i>p</i>
		Downregulated	Upregulated	
Age (years)				
<50	34 (100)	7 (21)	7 (21)	1.000 ^a
$\geq$ 50		10 (29)	10 (29)	
Menopause	31 (100)			
No		5 (16)	3 (10)	0.4331 ^a
Yes		10 (32)	13 (42)	
Histologic grade	34 (100)			
Low grade		3 (9)	3 (9)	1.000 ^b
High grade		14 (41)	14 (41)	
Clinical FIGO stage	34 (100)			0.4675 ^a
I		8 (21)	5 (18)	
II		2 (6)	3 (9)	
III		3 (9)	3 (9)	
IV		4 (12)	6 (18)	
Adjuvant therapy	34 (100)			0.6421 ^a
No		6 (18)	9 (25)	
Chemotherapy		7 (21)	6 (18)	
Radiotherapy		3 (9)	1 (3)	
Chemo and Radio		1 (3)	1 (3)	
Relapse	34 (100)			0.4646 ^b
No		7 (21)	4 (11)	
Yes		10 (30)	13 (38)	
Mitotic count (mitoses/10 high-power fields)	20 (100)			1.000 ^b
$\leq$ 10		1 (5)	2 (10)	
$\geq$ 10		9 (45)	8 (40)	
Metastasis	34 (100)			1.000 ^b
No		1 (3)	1 (3)	
Yes		16 (47)	16 (47)	
Metastasis Localization	26 (100)			0.2016 ^b
Local (pelvic)		2 (8)	6 (23)	
Distant		11 (42)	7 (27)	

^a Chi-square; ^b Fisher exact; FIGO, International Federation of Gynecology and Obstetrics.

Table S4. Comparison between clinical and pathological features and the *let-7b* expression.

Variables	n (%)	<i>let-7b</i>		<i>p</i>
		Downregulated	Upregulated	
Age (years)				
<50	34 (100)	6 (18)	8 (24)	0.1048 ^a
≥50		11 (32)	9 (26)	
Menopause	31 (100)			0.4125 ^b
No		5 (16)	3 (10)	
Yes		9 (29)	14 (45)	
Histologic grade	34 (100)			0.6562 ^b
Low grade		4 (12)	2 (6)	
High grade		13 (38)	15 (44)	
Clinical FIGO stage	34 (100)			0.7310 ^a
I		9 (26)	4 (12)	
II		2 (6)	3 (9)	
III		3 (9)	3 (9)	
IV		3 (9)	7 (20)	
Adjuvant therapy	34 (100)			0.6239 ^a
No		8 (23)	7 (21)	
Chemotherapy		5 (15)	8 (23)	
Radiotherapy		3 (9)	1 (3)	
Chemo and Radio		1 (3)	1 (3)	
Relapse	34 (100)			1.000 ^b
No		6 (18)	5 (15)	
Yes		11 (32)	12 (35)	
Mitotic count (mitoses/10 high-power fields)	20 (100)			1.000 ^b
≤10		1 (5)	2 (10)	
≥10		6 (30)	11 (55)	
Metastasis	34 (100)			0.4848 ^b
No		2 (6)	0 (0)	
Yes		15 (44)	17 (50)	
Metastasis Localization	23 (100)			0.1930 ^b
Local (pelvic)		2 (9)	6 (26)	
Distant		9 (39)	6 (26)	

^a Chi-square; ^b Fisher exact; FIGO, International Federation of Gynecology and Obstetrics.

Table S5. Comparison between clinical and pathological features and the *let-7c* expression.

Variables	n (%)	<i>let-7c</i>		<i>p</i>
		Downregulated	Upregulated	
Age (years)				
<50	34 (100)	6 (18)	8 (24)	0.7283 ^a
≥50		11 (32)	9 (26)	
Menopause	31 (100)			
No		4 (13)	4 (13)	1.000 ^b
Yes		11 (36)	12 (38)	
Histologic grade	34 (100)			
Low grade		3 (9)	3 (9)	1.000 ^b
High grade		14 (41)	14 (41)	
Clinical FIGO stage	34 (100)			0.4767 ^a
I		8 (23)	5 (14)	
II		3 (9)	2 (6)	
III		3 (9)	3 (9)	
IV		3 (9)	7 (21)	
Adjuvant therapy	34 (100)			0.1725 ^a
No		8 (23)	7 (21)	
Chemotherapy		4 (12)	9 (26)	
Radiotherapy		3 (9)	1 (3)	
Chemo and Radio		2 (6)	0 (0)	
Relapse	34 (100)			1.000 ^b
No		5 (14)	6 (18)	
Yes		12 (35)	11 (33)	
Mitotic count (mitoses/10 high-power fields)	20 (100)			0.5211 ^b
≤10		0 (0)	3 (15)	
≥10		7 (35)	10 (50)	
Metastasis	34 (100)			0.4848 ^b
No		2 (6)	0 (0)	
Yes		15 (44)	17 (50)	
Metastasis Localization	23 (100)			0.8994 ^b
Local (pelvic)		2 (9)	6 (26)	
Distant		10 (43)	5 (22)	

^a Chi-square; ^b Fisher exact; FIGO, International Federation of Gynecology and Obstetrics.

Table S6. Comparison between clinical and pathological features and the *let-7d* expression.

Variables	n (%)	<i>let-7d</i>		<i>p</i>
		Downregulated	Upregulated	
Age (years)				
<50	34 (100)	5 (15)	9 (26)	0.2960 ^b
≥50		12 (35)	8 (24)	
Menopause	31 (100)			
No		5 (16)	3 (10)	0.4331 ^b
Yes		10 (32)	13 (42)	
Histologic grade	34 (100)			
Low grade		4 (12)	2 (6)	0.6562 ^b
High grade		13 (38)	15 (44)	
Clinical FIGO stage	34 (100)			0.3238 ^a
I		7 (21)	6 (17)	
II		4 (11)	1 (3)	
III		3 (9)	3 (9)	
IV		3 (9)	7 (21)	
Adjuvant therapy	34 (100)			0.2985 ^a
No		6 (17)	9 (27)	
Chemotherapy		6 (17)	7 (21)	
Radiotherapy		3 (9)	1 (3)	
Chemo and Radio		2 (6)	0 (0)	
Relapse	34 (100)			0.4646 ^b
No		7 (21)	4 (11)	
Yes		10 (30)	13 (38)	
Mitotic count (mitoses/10 high-power fields)	20 (100)			1.000 ^b
≤10		1 (5)	2 (10)	
≥10		6 (30)	11 (55)	
Metastasis	34 (100)			0.4848 ^b
No		2 (6)	0 (0)	
Yes		15 (44)	17 (50)	
Metastasis Localization	23 (100)			0.0743 ^b
Local (pelvic)		1 (5)	7 (30)	
Distant		9 (39)	6 (26)	

^a Chi-square; ^b Fisher exact; FIGO, International Federation of Gynecology and Obstetrics.

Table S7. Comparison between clinical and pathological features and the *let-7e* expression.

Variables	n (%)	<i>let-7e</i>		<i>p</i>
		Downregulated	Upregulated	
Age (years)				
<50	34 (100)	5 (15)	9 (26)	0.2960 ^b
≥50		12 (35)	8 (24)	
Menopause	31 (100)			
No		5 (16)	3 (10)	0.4331 ^b
Yes		10 (32)	13 (42)	
Histologic grade	34 (100)			
Low grade		3 (9)	3 (9)	1.000 ^b
High grade		14 (41)	14 (41)	
Clinical FIGO stage	34 (100)			0.2930 ^a
I		9 (26)	4 (12)	
II		2 (6)	3 (9)	
III		3 (9)	3 (9)	
IV		3 (9)	7 (20)	
Adjuvant therapy	34 (100)			0.2887 ^a
No		7 (21)	8 (23)	
Chemotherapy		5 (15)	8 (23)	
Radiotherapy		3 (9)	1 (3)	
Chemo and Radio		2 (6)	0 (0)	
Relapse	34 (100)			0.7139 ^a
No		5 (15)	6 (18)	
Yes		12 (35)	11 (32)	
Mitotic count (mitoses/10 high-power fields)	20 (100)			1.000 ^b
≤10		1 (5)	2 (10)	
≥10		6 (30)	11 (55)	
Metastasis	34 (100)			1.000 ^b
No		1 (3)	1 (3)	
Yes		16 (47)	16 (47)	
Metastasis Localization	23 (100)			0.0094 ^b
Local (pelvic)		1 (5)	7 (30)	
Distant		11 (48)	4 (17)	

^a Chi-square; ^b Fisher exact; FIGO, International Federation of Gynecology and Obstetrics.

Table S8. Comparison between clinical and pathological features and the *let-7f* expression.

Variables	n (%)	<i>let-7f</i>		<i>p</i>
		Downregulated	Upregulated	
Age (years)				
<50	34 (100)	5 (15)	9 (26,5)	0.3151
≥50		11 (32)	9 (26,5)	
Menopause	31 (100)			
No		5 (16)	3 (10)	0.4125 ^b
Yes		9 (29)	14 (45)	
Histologic grade	34 (100)			
Low grade		4 (12)	2 (6)	0.3872 ^b
High grade		12 (35)	16 (47)	
Clinical FIGO stage	34 (100)			0.2223 ^a
I		8 (23)	5 (15)	
II		3 (9)	2 (6)	
III		3 (9)	3 (9)	
IV		2 (6)	8 (23)	
Adjuvant therapy	34 (100)			0.6488 ^a
No		7 (21)	8 (23)	
Chemotherapy		5 (15)	8 (23)	
Radiotherapy		3 (9)	1 (3)	
Chemo and Radio		1 (3)	1 (3)	
Relapse	34 (100)			0.7166 ^a
No		6 (17)	5 (15)	
Yes		10 (30)	13 (38)	
Mitotic count (mitoses/10 high-power fields)	20 (100)			1.000 ^b
≤10		1 (5)	2 (10)	
≥10		6 (30)	11 (55)	
Metastasis	34 (100)			0.2139 ^b
No		2 (6)	0 (0)	
Yes		14 (41)	18 (53)	
Metastasis Localization	23 (100)			0.3788 ^b
Local (pelvic)		2 (9)	6 (26)	
Distant		8 (35)	7 (30)	

^a Chi-square; ^b Fisher exact.

Table S9. Comparison between clinical and pathological features and the *let-7g* expression.

Variables	n (%)	<i>let-7g</i>		<i>p</i>
		Downregulated	Upregulated	
Age (years)				
<50	34 (100)	8 (24)	6 (18)	0.4858 ^a
≥50		9 (26)	11 (32)	
Menopause	31 (100)			0.6980 ^b
No		3 (10)	5 (16)	
Yes		11 (36)	12 (38)	
Histologic grade	34 (100)			1.000 ^b
Low grade		3 (9)	3 (9)	
High grade		14 (41)	14 (41)	
Clinical FIGO stage	34 (100)			0.1584 ^a
I		9 (27)	4 (12)	
II		3 (9)	2 (6)	
III		1 (3)	5 (15)	
IV		4 (11)	6 (17)	
Adjuvant therapy	34 (100)			0.6239 ^a
No		8 (23)	7 (21)	
Chemotherapy		5 (15)	8 (23)	
Radiotherapy		3 (9)	1 (3)	
Chemo and Radio		1 (3)	1 (3)	
Relapse	34 (100)			0.4646 ^b
No		7 (21)	4 (12)	
Yes		10 (29)	13 (38)	
Mitotic count (mitoses/10 high-power fields)	20 (100)			1.000 ^b
≤10		1 (5)	2 (10)	
≥10		7 (35)	10 (50)	
Metastasis	34 (100)			0.4848 ^b
No		2 (6)	0 (0)	
Yes		15 (44)	17 (50)	
Metastasis Localization	23 (100)			0.3788 ^b
Local (pelvic)		2 (9)	6 (26)	
Distant		8 (35)	7 (30)	

^a Chi-square; ^b Fisher exact; FIGO, International Federation of Gynecology and Obstetrics.

Table S10. Comparison between clinical and pathological features and the *let-7i* expression.

Variables	n (%)	<i>let-7i</i>		<i>p</i>
		Downregulated	Upregulated	
Age (years)				
<50	34 (100)	8 (24)	6 (18)	0.4858 ^a
≥50		9 (26)	11 (32)	
Menopause	31 (100)			0.6980 ^b
No		3 (10)	5 (16)	
Yes		11 (36)	12 (38)	
Histologic grade	34 (100)			0.6562 ^b
Low grade		2 (6)	4 (12)	
High grade		15 (44)	13 (38)	
Clinical FIGO stage	34 (100)			0.1584 ^a
I		9 (27)	4 (12)	
II		3 (9)	2 (6)	
III		1 (3)	5 (15)	
IV		4 (11)	6 (17)	
Adjuvant therapy	34 (100)			0.9861 ^a
No		8 (23)	7 (21)	
Chemotherapy		6 (17)	7 (21)	
Radiotherapy		2 (6)	2 (6)	
Chemo and Radio		1 (3)	1 (3)	
Relapse	34 (100)			1.000 ^a
No		6 (17)	5 (15)	
Yes		11 (33)	12 (35)	
Mitotic count (mitoses/10 high-power fields)	20 (100)			0.5211 ^b
≤10		0 (0)	3 (15)	
≥10		7 (35)	10 (50)	
Metastasis	34 (100)			0.4848 ^b
No		2 (6)	0 (0)	
Yes		15 (44)	17 (50)	
Metastasis Localization	23 (100)			0.1930 ^b
Local (pelvic)		2 (9)	6 (26)	
Distant		9 (39)	6 (26)	

^a Chi-square; ^b Fisher exact; FIGO, International Federation of Gynecology and Obstetrics.