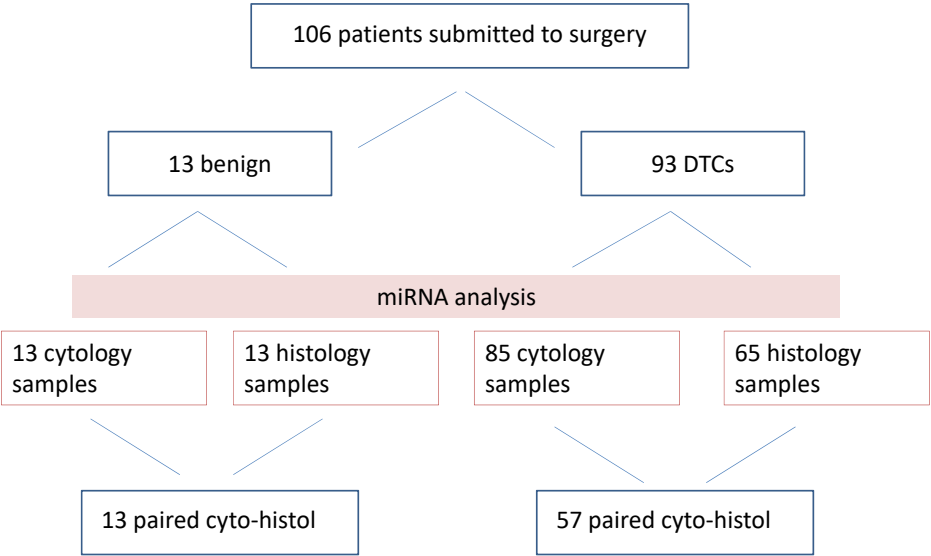


Supplementary Table S1. Series composition for miRNA analysis.



Supplementary Table 1. Series composition for miRNA analysis

Supplementary Table S2. MiRNAs expression in cytology samples by Bethesda categories in all series.

miRNAs in cytology	By Bethesda categories				
	n	Cytology	Median*	P25 - P75*	Min - Max value*
miRNA146	96				
	03	ND	0.005	0.000 - 0.000	0.000 –0.21
	20	Benign	0.161	0.071 – 1.339	0.000 – 853.8
	47	AUS + FN	0.756	0.079 – 7.395	0.000 – 1768,34
	26	SM+ M	1.275	0.004 – 138.81	0.000 – 1627.93
miRNA221	97				
	03	ND	0.062	0.000 – 0.000	0.000 –0.081
	20	Benign	0.237	0.062 – 1.802	0.000 – 11.033
	48	AUS + FN	0.169	0.043 – 1.095	0.000 – 51.976
	26	SM+ M	0.400	0.000 – 8.265	0.000 – 24.626
miRNA222	91				
	03	ND	0.903	0.000 –0.000	0.000 –1.501
	18	Benign	1.951	0.830 –5.545	0.000 – 1120.686
	44	AUS + FN	1.045	0.343 – 14.592	0.000 – 2604.770
	26	SM+ M	7.581	.004 – 121.022	0.000 – 1111.663
miRNA15a	98				
	03	ND	0.412	0.000 –0.000	0.000 – 0.772
	21	Benign	0.745	0.408 – 1.148	0.000 – 7.390
	48	AUS + FN	1.198	0.475 – 4.772	0.000 – 47.341
	26	SM+ M	0.691	0.000 – 2.629	0.000 – 7.831

\* The 2- $\Delta\Delta$ CT method was used to quantification of miRNA expression normalized to miR-16.

Legend: ND: Non-diagnostic, AUS: Atypia of Undetermined Significance, FN: Follicular Neoplasm, SM: Suspicious for malignancy and M: Malignant. P25-75: percentile 25 and percentile 75. Max-Min: maximum and minimum value.

MiRNAs expression in cytology	Histology diagnosis					
	n	Final Diagnosis	Median*	P25 - P75*	min - max value*	p-value
miRNA146	96					0.895
	11	Benign	0.308	0.141 - 1.530	0.086 - 4.394	
	85	Malignant	0.489	0.045 - 16.80	0.000 - 1768.34	
miRNA221	97					0.169
	11	Benign	0.535	0.155 - 2.351	0.035 - 5.242	
	86	Malignant	0.172	0.039 - 2.636	0.000 - 51.976	
miRNA222	97					0.402
	11	Benign	0.914	0.506 - 2.493	0.089 - 6.358	
	86	Malignant	1.460	0.330 - 32.199	0.000 - 2604,77	
miRNA15a	98					0.402
	11	Benign	1.053	0.745 - 4.349	0.016 - 7.390	

Supplementary Table S3. MiRNAs expression in cytology samples by histology diagnosis in all series.

	87	Malignant	0.686	0.415 – 2.999	0.000 - 47.341	
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\* The 2- $\Delta\Delta$ CT method was used to quantification of miRNA expression normalized to miR-16.

Legend: P25-75: percentile 25 and percentile 75. Max-min: maximum and minimum value

Supplementary Table S4. Five highest extreme frequencies of miRNAs expression in cytology samples by histology diagnosis in all series.

Histology diagnosis	Highest values of miRNAs expression* in cytology			
	miRNA-146	miRNA-221	miRNA-222	miRNA-15a
Benign	4.394	5.242	6.358	7.390
	2.881	3.978	3.139	5.620
	1.529	2.351	1.846	4.349
	0.770	1.401	1.384	1.242
	0.610	0.677	0.914	1.193
Malignant	1768.341	51.976	2604.770	47.341
	1627.930	48.630	1120.686	11.342
	1121.931	24.626	1112.533	10.989
	1041.914	16.130	1111.663	9.556
	958.423	11.653	1106.747	9.486

\* The 2- $\Delta\Delta$ CT method was used to quantification of miRNA expression normalized to miR-16.

Supplementary Table S5. MiRNAs expression in histology within histological subtypes in all series.

miRNAs in histology* n=106	Histological subtypes					
	Benign n=13	WDT-UMP n=2	NIFT n=4	PTC n=81	FTC n=4	HCC n=2
miRNA-146 n= 60 Median* P25-P75* Min – Max *	n=8 0.66 0.392 – 2.456 0.322 – 5.341	n=1 - - -	n=2 0.226 0.142 – 0. 0.142 – 0.310	n=46 65.667 8.351 – 1316.098 0.016 – 27755.752	n=2 0.227 – 0. 0.025 – 0. 0.025 – 0.428	n=1 - - -
miRNA-221 n= 76 Median* P25-P75* Min – Max*	n=10 1.312 0.781 – 1.798 0.192 – 4.395	n=1 - - -	n=4 1.918 0.385 – 4.092 0.012 – 4.678	n=57 5.45 1.582 – 10.900 0.368 – 63.304	n=2 0.115 0.108 – 0. 0.108 – 0.124	n=2 6.278 3.297 – 0. 3.297 – 9.260
miRNA-222 n= 78 Median* P25-P75* Min – Max*	n=10 1.067 0.645 – 2.544 0.328 – 4.348	n=1 - - -	n=4 2.465 0.626 – 9.693 0.271 – 11.843	n=59 3.511 1.183 – 13.315 0.115 – 3006.7	n=2 0.134 0.124 – 0. 0.124 – 0.143	n=2 16.21 7.7 – 0. 7.7 – 0. 24.72
miRNA-15a n= 77 Median* P25-P75* Min – Max*	n=10 0.683 0.510 – 1.610 0.282 – 2.514	n=1 - - -	n=4 1.020 0.835 – 2.177 0.779 – 2.556	n=58 2.682 1.396 – 37.388 0.479 – 99.641	n=2 1.594 1.439 – 0. 1.439 – 1.747	n=2 0.236 0.231 – 0. 0.231 – 0.241

\* The 2- $\Delta\Delta$ CT method was used to quantification of miRNA expression normalized to miR-16.

Legend: WDT-UMP: Well differentiated thyroid tumor of uncertain malignant potential; NIFT: noninvasive follicular thyroid neoplasm with papillary-like nuclear features; PTC: papillary thyroid carcinoma; FTC: follicular thyroid carcinoma; HCC: Hürthle cell carcinoma: not available data to estimate summary measures. P25-75: percentile 25 and percentile 75. Max-min: maximum and minimum value

Supplementary Table S6. Association of the miRNAs expression levels and the presence of genetic mutations in cytology samples in PTCs.

Genetic mutations in Cytology	miRNAs in Cytology							
	miRNA-146		miRNA-221		miRNA-222		miRNA-15a	
	n	Median*	n	Median*	n	Median*	n	Median*
<i>TERTp</i>	84		85		80		86	
Absent	74	0.619	75	0.247	70	1.460	76	0.765
Present	10	0.880	10	0.170	10	0.963	10	2.044
p-value		0.730		0.754		0.391		0.609
<i>BRAF</i>	84		85		80		86	
Absent	62	0.619	63	0.198	58	1.133	64	1.123
Present	22	0.905	22	0.341	22	3.709	22	0.589
p-value		0.555		0.779		0.338		0.135
<i>RAS</i>	83		84		79		86	
Absent	64	0.696	65	0.266	61	1.420	66	0.801
Present	19	0.219	19	0.191	18	1.010	19	1.204
p-value		0.193		0.096		0.082		0.792

\* The 2- $\Delta\Delta$ CT method was used to quantification of miRNA expression normalized to miR-16.

Legend: *TERTp*: telomerase reverse transcriptase promoter; *BRAF*: B-Raf proto-oncogene, serine/threonine kinase; *NRAS*: NRAS proto-oncogene, GTPase; *HRAS*: HRas proto-oncogene, GTPase, and *KRAS*—*KRAS* proto-oncogene, GTPase.

Supplementary Table S7. A. Associations between miR-146b expression and clinicopathological features in Papillary Thyroid Carcinomas.

miR-146b and clinicopathological characteristics n =54 (100%)	Median*	P25 - P75*	Min - Max value*	p-value
Mean tumor size (SD) (mm) (n=54)	-	-	-	0.179
Extra thyroidal extension Absent 42 (77.8) Present 12 (22.2)	27.227 147.041	3.127 - 389.557 3.333 - 1402.208	0.016 - 6476.520 0.473 - 27755.768	0.318
Capsule invasion Absent 29 (53.7) Present 25 (46.3)	8.733 126.683	1.131 - 119.808 20.400 - 1377.380	0.016 - 5276.991 0.473 - 27755.768	<b>0.011</b>
Vascular invasion Absent 45 (83.3) Present 9 (16.7)	27.945 95.902	3.119 - 448.500 13.774 - 2771.874	0.016 - 6476.520 0.473 - 27755.768	0.270
Lymphatic invasion Absent 48 (88.9) Present 6 (11.1)	29.856 732.253	3.215 - 532.402 1.215 - 10022.989	0.016 - 6476.520 0.473 - 27755.768	0.475
Psammoma bodies Absent 47 (87) Present 7 (13)	22.303 160.507	3.006 - 616.304 61.201 - 5276.991	0.016 - 6476.520 32.819 - 27755.768	<b>0.019</b>
Calcifications Absent 43 (79.6) Present 11 (20.4)	22.303 160.507	2.725 - 280.695 32.819 - 5276.991	0.016 - 5268.565 7.207 - 27755.768	<b>0.010</b>
Lymph node metastases Absent 49 (90.7) Present 05 (9.3)	32.819 3.070	3.740 - 843.629 0.968 - 746.444	0.016 - 27755.768 0.473 - 1431.686	0.350

\* The 2- $\Delta\Delta$ CT method was used to quantification of miRNA expression normalized to miR-16.

Legend: P25-75: percentile 25 and percentile 75. Max-min: maximum and minimum value.



Supplementary Table S7. B. Associations between miR-221 expression and clinicopathological features in Papillary Thyroid Carcinomas.

miR-221 and clinicopathological characteristics n =67 (100%)	Median*	P25 - P75*	Min - Max value*	p-value
Mean tumor size (SD) (mm) n =67	-	-	-	0.817
Extra thyroidal extension Absent 54 (80.6) Present 13 (19.4)	2.727 7.786	1.034 - 9.257 2.223 - 14.415	0.192 - 36.928 1.545 - 63.304	0.078
Capsule invasion Absent 39 (58.2) Present 28 (41.8)	1,618 8.064	0.878 - 6.802 2.855 - 15.441	0.192 - 18.908 0.368 - 63.304	<b>&lt;0.001</b>
Vascular invasion Absent 56 (83.6) Present 11 (16.4)	2.355 12.518	1.068 - 8,065 5.452 - 23,279	0.192 - 34.725 2.342 - 2.342	<b>&lt;0.001</b>
Lymphatic invasion Absent 60 (89.6) Present 7 (10.4)	2.900 16.415	1.240 - 1240 1.820 - 23.279	0.192 - 36.928 0.368 - 63.304	0.078
Oncocytic component Absent 58 (86.6) Present 9 (13.4)	2.342 12.414	1.070 - 7.972 8,283 - 28.598	3.006 - 616.304 5.452 - 63.304	<b>0.002</b>
Calcifications Absent 54 (80.6) Present 13 (19.4)	2.403 8.224	1.072 - 8.126 3.376 - 16.974	0.192 - 63.304 0.368 - 23.279	<b>0.031</b>
Lymph node metastases Absent 61 (91) Present 06 (9)	3.190 5.413	1.145 - 10.018 1,751 - 11.378	0.192 - 63.304 1.545 - 17.532	0.499

\* The 2- $\Delta\Delta$ CT method was used to quantification of miRNA expression normalized to miR-16.

Legend: P25-75: percentile 25 and percentile 75. Max-min: maximum and minimum value

Supplementary Table S7.C. Associations between miR-222 expression and clinicopathological features in Papillary Thyroid Carcinomas.

miR-222 and clinicopathological characteristics n =69 (100%)	Median*	P25 - P75*	Min - Max value*	p-value
Mean tumor size (SD) (mm) (n=69)	-	-	-	0.253
Extra thyroidal extension Absent 56 (81.2) Present 13 (18.8)	2.210 14.006	0.870 - 5.603 4.238 - 36.416	0.114 - 43,231 0.908 - 3006.772	<b>&lt;0.001</b>
Capsule invasion Absent 39 (56.5) Present 30 (43.5)	1.669 5.284	0.717 - 4.347 2.014 - 14.113	0.114 - 68.403 0.861 - 3006.772	<b>0.005</b>
Vascular invasion Absent 57 (82.6) Present 12 (17.4)	2.222 10.575	0.879 - 4.806 7.220 - 38.986	0.114 - 68,403 1.392 - 3006.772	<b>&lt;0.001</b>
Lymphatic invasion Absent 61 (88.4) Present 8 (11.6)	2.325 8.172	0.902 - 8.224 3.840 - 36.370	0.114 - 68.403 1.392 - 3006.772	<b>0.020</b>
Psammoma bodies Absent 58 (84) Present 11 (16)	2.251 8.230	0.888 - 7.806 3.465 - 15.210	0.114 - 68.403 1,392 - 3006.772	<b>0.010</b>
Calcifications Absent 55 (79.7) Present 14 (20.3)	2.222 7.949	0.861 - 5.921 3.102 - 19.672	0.114 - 68,403 1.392 - 3006.772	<b>0.006</b>
Oncocytic component Absent 50 (72.5) Present 19 (27.5)	1.775 13.211	0.843 - 6.496 3.673 - 32.168	0.114 - 3006,772 2,222 - 41.556	<b>0.008</b>
Inflammatory infiltrate Absent 50 (72.5) Present 19 (27.5)	2.040 4.965	0.888 - 7.806 3.354 - 16.633	0.114 - 68.403 0.429 - 3006.772	<b>0.019</b>
Tall cells Absent 59 (85.5) Present 10 (14.5)	2.222 8.230	0.897 - 8.219 4.055 - 36.352	0.114 - 68,403 3.354 - 3006.772	<b>0.017</b>
Focality Unifocal 40 (58) Multifocal 29 (42)	3.200 7.070	1.000 - 7.669 1.475 - 27.044	0.114 - 68.403 0.196 - 3006.772	<b>0.049</b>
Lymph node metastases Absent 62 (89.9) Present 07 (10.1)	3.093 4.965	0.951 - 12.659 1.392 - 8.675	0.114 - 3006.772 0.908 - 41.556	0.330

\* The 2- $\Delta\Delta$ CT method was used to quantification of miRNA expression normalized to miR-16.

Legend: P25-75: percentile 25 and percentile 75. Max-min: maximum and minimum value.

Supplementary Table S7. D. Associations between miR-15a expression and clinicopathological features in Papillary Thyroid Carcinomas.

miR-15a and clinicopathological characteristics n =68 (100%)	Median*	P25 - P75*	Min - Max value*	p-value
Mean tumor size (SD) (mm) (n=68)	-	-	-	0.649
Extra thyroidal extension Absent 56 (82.4) Present 12 (17.6)	2.210 1.333	1.309 - 37.281 1.194 - 3.570	0.282 - 99.640 0.847- 52.086	0.182
Capsule invasion Absent 39 (57.4) Present 29 (42.6)	1.577 19.882	0.881 - 4.089 1.527- 41.928	0.282 - 81,366 0.712 - 99.640	<b>0.006</b>
Focality Unifocal 39 (57.4) Multifocal 29 (42.6)	1.867 2.561	1.249 - 37.278 1.745 - 38.385	0.473 - 99.640 0.712 - 55.047	<b>0.041</b>
Lymph node metastases Absent 61 (89.7) Present 07 (10.3)	2.475 1.374	1.263 - 37.257 0.935 - 19.882	0.282 - 99.640 0.847 - 37.705	0.380

\* The 2- $\Delta\Delta$ CT method was used to quantification of miRNA expression normalized to miR-16.

Legend: P25-75: percentile 25 and percentile 75. Max-min: maximum and minimum value