

## Comparative transcriptome analyses highlight distinct pathogenetic mechanisms for pleuropulmonary blastoma and congenital pulmonary airway malformations

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### SUPPLEMENTAL DATA

#### SUPPLEMENTAL TABLES

**Supplementary Table S1. General characteristics of patients.**

N° Patient	Diagnosis	Age at tissue collection (months)	Sex	<i>DICER1</i> status	<i>KRAS</i> status
CTL1	Normal lung	na	♂	wt	nd
CTL2	Pulmonary arterial hypertension	2 days	♂	wt	nd
CTL3	Pulmonary arterial hypertension	54	♂	wt	nd
CTL4	Normal Lung	21	♀	wt	nd
CTL5	Normal tissue flanking CPAM pathological tissue	15	♂	nd	wt
CTL6	Normal tissue flanking CPAM pathological tissue	6	♂	nd	wt
CTL7	Normal lung	na	na	nd	nd
CTL8	Normal lung	na	na	nd	nd
CPAM1	CPAM	15	♂	wt	wt
CPAM2	CPAM (Type 1)	2	♂	wt	c.35G>T (p.G12V)
CPAM3	CPAM (Type 2)	6	♀	c.5504A>G (p.Y1835C)	wt
CPAM4	CPAM (Type 2)	12	♂	wt	wt
CPAM5	CPAM	8	♀	nd	wt
CPAM 6	CPAM	11	♀	nd	wt
CPAM7	CPAM	11	♀	nd	wt
CPAM8	CPAM (Type 1)	21	na	nd	wt
CPAM9	CPAM (Type 1)	18	na	nd	wt
CPAM10	CPAM (Type 1)	18	na	nd	wt

CPAM11	CPAM (Type 1)	20	na	nd	wt
CPAM12	CPAM	21	♀	nd	wt
CPAM13	CPAM (Type 2)	6	na	nd	wt
CPAM14	CPAM	15	♂	nd	wt
CPAM15	CPAM	7	♂	nd	c.35G>A (p.G12D)
CPAM16	CPAM	10	♀	nd	c.35G>T (p.G12V)
CPAM17	CPAM	6	♀	nd	c.35G>A (p.G12D)
CPAM18	CPAM	6	♂	nd	c.35G>A (p.G12D)
CPAM19	CPAM (Type 1)	22	na	nd	c.35G>A (p.G12D)
CPAM20	CPAM	na	na	nd	c.35G>A (p.G12D)
CPAM21	CPAM (Type 1)	1 day	♀	nd	c.35G>A (p.G12D)
CPAM22	CPAM	21	♀	nd	c.35G>A (p.G12D)
CPAM23	CPAM (Type 1)	1 day	♂	nd	c.35G>A (p.G12D)
CPAM24	CPAM	25	♀	nd	c.35G>A (p.G12D)
CPAM25	CPAM	12	♂	nd	c.35G>A (p.G12D)
<b>PPB1</b>	PPB	39	♂	Mutation 1: c.4403_4406delCTCT, (p.S1468Ffs*21) Mutation 2: c.5439G>T, (p.E1813D)	c.562A>G (p.I188V)
<b>PPB2</b>	PPB (Type II)	28	♀	c.5428G>T, (p.D1810Y)	wt
<b>PBB3</b>	PPB (Type I)	12	♂	Mutation 1: c.826_838delGAAGCACTTAATT, (p.E276Lfs*18) Mutation 2: c.5125G>A, (p.D1709N)	wt
<b>PPB4</b>	PPB	36	♀	Germline: c.940_941delGG, (p.G314Tfs*6) Somatic: c.5113G>A, (p.E1705K)	wt
PPB5	PPB (Type II)	24	na	c.2379T>G (p.Y793*)	nd
PPB6	PPB (Type II)	36	na	negative	nd
PPB7	PPB (Type III)	45	♂	nd	nd
PPB8	PPB (Type III)	48	na	Germline: c.4407_4410 delTTCT (p.L1469Lfs*20)	nd
PPB9	PPB (Type II)	23	na	Germline: c.3505insT (p.S1169Ffs*8) Somatic: c.5438A>G (p.E1813G)	nd
PPB10	PPB (Type II)	24	na	Germline: c.5125G>A (p.D1709N)	nd
PPB11	PPB (Type III)	48	na	Somatic: c.5125G>A (p.D1709N)	nd
PPB12	PPB (Type II)	36	na	c.5392delA (p.K1798Kfs*40)	nd
PPB13	PPB (Type I)	10 days	na	Germline: c.5439G>C (p.E1813D)	nd
PPB14	PPB (Type III)	36	na	c.2040+1G>T (p.G681C)	nd

na: not available

nd: not determined

**Supplementary Table S2. List of primary and secondary antibodies.**

<b>Antigen</b>	<b>Antibody/clone</b>	<b>Reference</b>	<b>Source</b>	<b>Dilution</b>
EED	rabbit monoclonal / E4L6E	85322	Cell Signaling	1/50
FOXA1	rabbit monoclonal / EPR10881-14	ab173287	Abcam	1/2000
FOXJ1	rabbit monoclonal / EPR21874	ab235445	Abcam	1/4000
Ki-67	mouse monoclonal / clone MM1	NCL-LKi67-MM1	Leica Biosystems	1/200
SIX1	rabbit monoclonal / D5S2S	16960	Cell Signaling	1/100
SOX2	rabbit monoclonal / C70B1	3728	Cell Signaling	1/100
TP63	rabbit polyclonal / H-137	sc-8343	Santa Cruz	1/50
Uteroglobin (CC10)	rabbit monoclonal / EPR27144-86	ab307666	Abcam	1/4000
Biotin-SP-conjugated goat anti-mouse IgG (H+L)		115-065-003	Cedarlane	1/250
Biotin-SP-conjugated goat anti-rabbit IgG (H+L)		111-065-003	Cedarlane	1/250

**Supplementary Table S3. RNA-seq, miRNA-seq and whole exome statistics.****A. RNA-seq statistics**

<b>Specimen</b>	<b>Reads</b>	<b>Number of reads generated</b>	<b>Number of reads after filtering</b>	<b>Number of uniquely mapped reads</b>	<b>% of uniquely mapped reads</b>	<b>% successfully assigned alignments</b>
CTL1	Paired-end	47918743	45803582	36476745	79.6	46.7
CTL2	Paired-end	43826362	41639129	34365526	82.5	42.8
CTL3	Paired-end	39078805	36893293	29810239	80.8	39.3
CTL4	Paired-end	38565527	37101395	32120602	86.6	36.7
CPAM1	Paired-end	39409708	37462903	30699410	81.9	38.7
CPAM2	Paired-end	36081526	34563643	29550661	85.5	40.6
CPAM3	Paired-end	30031118	27405158	21437740	78.2	47.6
CPAM4	Paired-end	28061596	25971525	21189207	81.6	36.5
PPB1	Paired-end	39377675	37867776	31223067	82.5	41.3
PPB2	Paired-end	36665840	35149612	27646718	78.7	40.6
PPB3	Paired-end	54454460	51518207	39610380	76.9	41.6
PPB4	Paired-end	31899613	31120497	26820942	86.2	74.7

**B. miRNA-seq statistics**

<b>Specimen</b>	<b>Reads</b>	<b>Number of reads generated</b>	<b>Number of reads after filtering</b>	<b>Number of mapped reads</b>	<b>% of reads mapped to genome</b>	<b>% successfully assigned alignments</b>
CTL1	Single-end	19795113	16981825	16939970	99.8	89.1
CTL2	Single-end	24246160	21345409	21287533	99.7	85.6
CTL3	Single-end	35447949	13386222	13319862	99.5	88.1
CTL4	Single-end	21275171	18936886	18888016	99.7	90.2
PPB1	Single-end	28872085	21426082	21363260	99.7	84.3
PPB2	Single-end	22306529	13679110	13646186	99.8	60.1
PPB3	Single-end	29443028	17212254	17127703	99.5	87.7

**C. Whole exome statistics**

<b>Specimen</b>	<b>Reads</b>	<b>Number of reads generated</b>	<b>Number of reads after filtering</b>	<b>Number of mapped reads</b>	<b>% of reads mapped to genome</b>	<b>% successfully assigned alignments to exome</b>
PPB1	Paired-end	31227991	30799338	30647205	99.5	79.0
PPB2	Paired-end	38259461	37691690	37473800	99.4	76.9
PPB3	Paired-end	38091308	37631363	37443649	99.5	78.7
PPB4	Paired-end	42947987	42395335	42186862	99.5	78.1

Supplementary Table S5. miRNA-seq data - miRNA expression PPB-CTL.

log2FC ≥1. padj≤0.05					
Gene	log2FoldChange	p value	padj	Mean RPM PPB	Mean RPM CTL
hsa-miR-490-5p	-6.75	3.01E-06	6.78E-05	0	1.26
hsa-miR-519a-3p	-6.61	5.42E-04	4.92E-03	0	1.12
hsa-miR-1283	-5.90	3.59E-04	3.52E-03	0.02	1.34
hsa-miR-1247-5p	-5.57	4.83E-06	9.40E-05	0.41	16.89
hsa-miR-6811-5p	-5.15	1.50E-03	1.10E-02	0	0.42
hsa-miR-516a-5p	-5.06	2.46E-05	4.08E-04	0.54	13.25
hsa-miR-2681-5p	-4.82	1.95E-03	1.33E-02	0.02	0.62
hsa-miR-4758-3p	-4.73	1.87E-03	1.31E-02	0.02	0.61
hsa-miR-5188	-4.70	6.68E-03	3.25E-02	0	0.31
hsa-miR-519a-5p	-4.65	3.23E-03	1.90E-02	0.09	1.69
hsa-miR-4705	-4.37	3.59E-04	3.52E-03	0.07	1.13
hsa-miR-1298-5p	-4.22	2.23E-03	1.44E-02	0.41	5.41
hsa-miR-346	-3.95	5.07E-03	2.65E-02	0.06	0.64
hsa-miR-522-3p	-3.91	2.02E-03	1.36E-02	0.24	2.99
hsa-miR-218-5p	-3.77	9.03E-07	2.48E-05	359.06	4244.1
hsa-miR-135a-5p	-3.65	4.36E-07	1.41E-05	2.66	25.97
hsa-miR-9983-3p	-3.44	6.09E-05	8.81E-04	2.16	18.62
hsa-miR-551b-3p	-3.43	6.70E-06	1.20E-04	1.41	13.23
hsa-miR-551b-5p	-3.29	5.95E-03	2.96E-02	0.1	0.81
hsa-miR-30d-5p	-3.10	3.24E-06	7.00E-05	4389.87	29396.4
hsa-miR-10a-5p	-3.10	2.74E-05	4.48E-04	2249.77	15539.4
hsa-miR-509-3-5p	-2.97	5.14E-03	2.67E-02	1.3	8.57
hsa-miR-133a-5p	-2.86	1.52E-03	1.10E-02	0.36	2.34
hsa-miR-1468-5p	-2.84	2.67E-03	1.65E-02	0.67	3.89
hsa-miR-125a-5p	-2.82	2.12E-04	2.26E-03	1412.46	7430.76
hsa-miR-511-5p	-2.78	4.43E-03	2.43E-02	36.67	216.74
hsa-miR-195-5p	-2.75	2.25E-05	3.79E-04	155.2	872.75
hsa-miR-548ba	-2.69	4.81E-03	2.55E-02	0.22	1.21
hsa-miR-146b-5p	-2.68	1.09E-03	8.45E-03	2473.66	13324.83
hsa-miR-335-5p	-2.68	6.67E-07	1.98E-05	79.74	418.82
hsa-miR-652-5p	-2.63	3.09E-03	1.82E-02	0.69	3.41
hsa-miR-30a-5p	-2.59	3.41E-04	3.47E-03	4025.64	19375.18
hsa-miR-30b-5p	-2.59	1.21E-04	1.49E-03	621.94	3010.75
hsa-miR-100-5p	-2.55	1.52E-03	1.10E-02	2795.74	14385.7
hsa-miR-199a-5p	-2.54	3.48E-04	3.51E-03	1089.99	5348.2

hsa-miR-30c-5p	-2.52	5.13E-04	4.75E-03	1311.13	5759.39
hsa-miR-181c-5p	-2.52	3.32E-04	3.40E-03	11.1	49.08
hsa-miR-101-5p	-2.52	1.91E-03	1.31E-02	0.5	2.61
hsa-miR-618	-2.51	4.62E-03	2.48E-02	4.42	17.78
hsa-miR-497-5p	-2.43	2.08E-04	2.26E-03	48.87	214.12
hsa-miR-145-5p	-2.40	6.47E-04	5.57E-03	835.35	3405.44
hsa-miR-455-5p	-2.39	1.00E-04	1.30E-03	254.43	1067.55
hsa-miR-3617-5p	-2.39	9.88E-03	4.47E-02	0.45	1.81
hsa-miR-125b-5p	-2.38	3.68E-03	2.10E-02	972.93	4047.49
hsa-miR-4636	-2.32	1.08E-02	4.79E-02	0.38	1.48
hsa-miR-218-1-3p	-2.29	1.09E-04	1.38E-03	3.05	11.84
hsa-miR-4683	-2.29	2.43E-03	1.53E-02	2.64	10.01
hsa-miR-181d-5p	-2.28	2.15E-03	1.42E-02	48.45	174.7
hsa-miR-5193	-2.26	6.35E-03	3.11E-02	0.35	1.34
hsa-miR-26a-5p	-2.25	2.70E-03	1.65E-02	24002.09	87083.82
hsa-miR-194-5p	-2.18	1.08E-03	8.37E-03	56.65	196.64
hsa-miR-99b-5p	-2.14	2.22E-04	2.34E-03	1410.25	4952.68
hsa-miR-30a-3p	-2.10	1.85E-04	2.07E-03	465.72	1610.53
hsa-miR-222-3p	-2.09	3.77E-03	2.12E-02	347.26	1106.61
hsa-miR-190a-5p	-2.09	2.20E-03	1.42E-02	1.43	5.02
hsa-miR-342-5p	-2.09	4.47E-03	2.44E-02	13.59	49.38
hsa-miR-130a-5p	-2.07	1.03E-02	4.63E-02	2.35	8.31
hsa-miR-3934-5p	-2.04	9.01E-03	4.15E-02	1.25	4.37
hsa-let-7e-5p	-2.03	5.45E-04	4.92E-03	345.16	1133.7
hsa-miR-296-5p	-2.02	6.12E-03	3.03E-02	2.42	7.49
hsa-miR-8062	-1.99	1.76E-03	1.26E-02	1.1	3.47
hsa-miR-328-3p	-1.99	6.13E-04	5.40E-03	120.96	376.21
hsa-let-7d-5p	-1.98	1.90E-03	1.31E-02	460.79	1407.92
hsa-miR-129-5p	-1.95	5.21E-03	2.68E-02	2.47	7.14
hsa-miR-192-5p	-1.94	2.43E-03	1.53E-02	192.32	560.53
hsa-miR-126-3p	-1.90	8.86E-04	7.29E-03	44420.12	134267.59
hsa-miR-1306-5p	-1.87	2.92E-03	1.75E-02	1.47	4.36
hsa-miR-26b-5p	-1.86	6.77E-03	3.27E-02	3483.88	9983.59
hsa-miR-576-5p	-1.83	7.42E-03	3.56E-02	6	16.81
hsa-miR-628-5p	-1.77	1.99E-03	1.34E-02	4.87	13.57
hsa-let-7b-5p	-1.73	1.08E-02	4.79E-02	4430.25	11637.24
hsa-miR-24-2-5p	-1.67	7.45E-03	3.56E-02	103.16	276.57
hsa-miR-504-5p	-1.62	5.17E-03	2.67E-02	26.73	64.99
hsa-miR-877-5p	-1.55	8.43E-03	3.95E-02	3.57	8.45

hsa-miR-99a-5p	-1.50	2.50E-03	1.56E-02	12967.26	30120.57
hsa-miR-143-3p	-1.47	5.81E-03	2.93E-02	65943.69	147287.86
hsa-miR-152-3p	1.51	6.19E-03	3.05E-02	6000.32	1819.07
hsa-miR-340-3p	1.52	4.53E-03	2.45E-02	209.81	59.43
hsa-miR-330-3p	1.64	5.90E-03	2.96E-02	107.48	27.55
hsa-miR-148b-3p	1.77	4.69E-03	2.50E-02	8919.52	2273.91
hsa-miR-1306-3p	1.81	8.91E-03	4.14E-02	9.12	2.2
hsa-miR-625-3p	1.88	1.02E-02	4.58E-02	69.4	16.3
hsa-miR-425-3p	1.89	5.55E-03	2.83E-02	324.99	76.76
hsa-miR-615-3p	1.91	2.35E-03	1.50E-02	31	6.75
hsa-miR-1343-3p	1.96	6.79E-03	3.27E-02	9.91	2.25
hsa-miR-1277-3p	1.97	8.53E-03	3.98E-02	17.38	3.51
hsa-let-7i-3p	2.06	1.18E-03	9.03E-03	99.84	20.6
hsa-miR-576-3p	2.13	5.69E-04	5.09E-03	23.72	4.66
hsa-miR-3177-3p	2.22	4.05E-03	2.25E-02	5.61	1.06
hsa-miR-4791	2.31	4.70E-03	2.50E-02	6.24	1.13
hsa-miR-320a-3p	2.32	4.41E-03	2.43E-02	5598.84	1005.45
hsa-miR-21-3p	2.38	2.12E-03	1.41E-02	427.22	71.56
hsa-miR-411-3p	2.41	1.02E-02	4.60E-02	42.81	6.32
hsa-miR-3613-3p	2.45	5.41E-04	4.92E-03	17.98	2.85
hsa-miR-2277-3p	2.49	8.05E-03	3.81E-02	3.37	0.53
hsa-miR-548a-3p	2.51	2.81E-03	1.70E-02	4.82	0.72
hsa-miR-185-3p	2.52	1.86E-03	1.30E-02	123.34	18.66
hsa-let-7f-2-3p	2.54	2.66E-03	1.65E-02	139.21	21.31
hsa-miR-323b-3p	2.56	1.07E-03	8.37E-03	22.4	2.95
hsa-miR-5001-3p	2.64	1.85E-03	1.30E-02	13.73	1.88
hsa-miR-4474-3p	2.64	3.02E-03	1.80E-02	3.17	0.45
hsa-miR-502-3p	2.69	2.88E-04	3.01E-03	500.56	66.99
hsa-miR-1262	2.74	3.42E-03	1.97E-02	5.79	0.78
hsa-miR-140-3p	2.75	5.82E-03	2.93E-02	15209.75	2091.54
hsa-let-7f-1-3p	2.77	6.90E-04	5.89E-03	244.44	31.07
hsa-let-7a-3p	2.79	5.54E-05	8.23E-04	2133.69	261.85
hsa-miR-944	2.81	4.50E-04	4.30E-03	5.01	0.55
hsa-miR-320c	2.84	1.50E-03	1.10E-02	125.49	16.11
hsa-miR-582-3p	2.87	3.57E-04	3.52E-03	658.27	82.72
hsa-miR-376c-3p	2.87	9.00E-03	4.15E-02	140.8	16.68
hsa-miR-624-3p	2.87	9.11E-03	4.18E-02	1.02	0.12
hsa-miR-320b	2.90	4.75E-04	4.51E-03	586.07	71.24
hsa-miR-543	2.93	3.39E-03	1.96E-02	439.34	43.62



hsa-miR-940	2.95	1.35E-03	1.01E-02	7.83	0.91
hsa-miR-487b-3p	2.98	3.71E-03	2.10E-02	247.56	24.19
hsa-miR-181a-3p	2.98	1.91E-07	6.52E-06	1214.74	134.06
hsa-miR-34a-3p	2.98	8.38E-05	1.11E-03	8.85	0.99
hsa-miR-190a-3p	2.98	3.85E-03	2.15E-02	2.01	0.22
hsa-miR-329-3p	3.00	2.44E-03	1.53E-02	150.65	14.59
hsa-miR-3620-3p	3.01	1.59E-03	1.14E-02	5.38	0.6
hsa-miR-539-3p	3.01	8.00E-03	3.81E-02	87.14	8.06
hsa-miR-339-3p	3.04	7.81E-05	1.08E-03	1063.02	115.8
hsa-miR-632	3.12	8.77E-04	7.27E-03	3.2	0.32
hsa-miR-17-3p	3.17	1.61E-04	1.84E-03	102.58	9.97
hsa-miR-376a-3p	3.18	1.83E-03	1.30E-02	88.72	8.13
hsa-miR-181c-3p	3.20	2.11E-04	2.26E-03	391.62	37.86
hsa-miR-660-3p	3.20	5.68E-05	8.32E-04	16.71	1.59
hsa-miR-4429	3.21	2.19E-03	1.42E-02	2.96	0.28
hsa-miR-382-3p	3.23	5.89E-04	5.23E-03	234.52	19.62
hsa-miR-136-3p	3.26	4.94E-03	2.59E-02	780.93	68.91
hsa-miR-205-5p	3.27	5.48E-03	2.81E-02	1114.25	80.43
hsa-miR-137-3p	3.28	6.62E-03	3.23E-02	1.4	0.14
hsa-miR-301a-3p	3.28	7.09E-04	6.01E-03	27.28	2.53
hsa-miR-494-3p	3.31	3.32E-03	1.93E-02	474.23	35.19
hsa-miR-9903	3.33	1.41E-04	1.69E-03	12.11	1.08
hsa-miR-488-3p	3.33	8.30E-04	6.94E-03	11.73	1.01
hsa-miR-10396b-5p	3.35	3.08E-03	1.82E-02	2.46	0.21
hsa-miR-26a-2-3p	3.36	1.03E-04	1.33E-03	132.73	11.79
hsa-miR-3149	3.36	9.37E-03	4.28E-02	1.03	0.08
hsa-miR-26a-1-3p	3.39	2.02E-04	2.23E-03	13.11	1.14
hsa-miR-665	3.39	5.13E-04	4.75E-03	7.3	0.56
hsa-miR-532-3p	3.40	1.81E-05	3.09E-04	332.42	27.87
hsa-miR-4286	3.43	8.40E-05	1.11E-03	10.17	0.85
hsa-miR-154-3p	3.44	7.35E-04	6.18E-03	22.52	1.73
hsa-miR-485-3p	3.45	4.85E-04	4.56E-03	113.12	8.1
hsa-miR-377-3p	3.46	1.22E-03	9.26E-03	58.39	4.23
hsa-miR-769-3p	3.47	3.30E-06	7.00E-05	39.03	3.09
hsa-miR-4741	3.47	5.76E-03	2.93E-02	1.82	0.14
hsa-miR-495-3p	3.48	1.03E-03	8.17E-03	782.42	55.35
hsa-miR-127-3p	3.51	1.34E-03	1.01E-02	14505.28	984.39
hsa-miR-4522	3.57	4.83E-03	2.55E-02	1.92	0.15
hsa-miR-675-3p	3.58	1.02E-03	8.17E-03	72.95	5.6

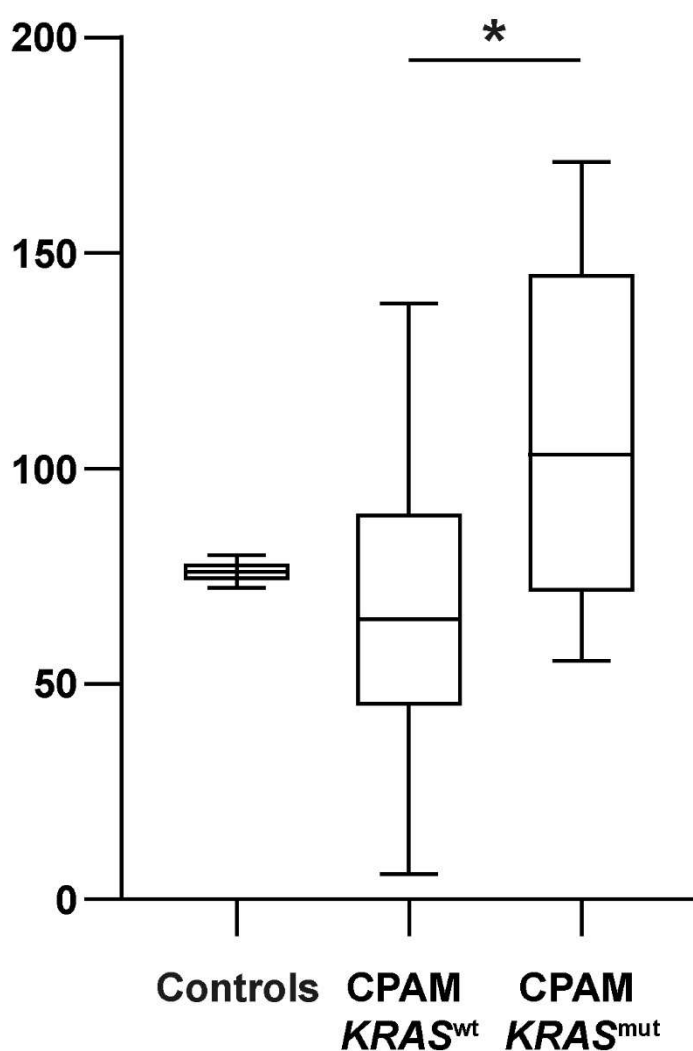
hsa-miR-381-3p	3.59	6.21E-04	5.43E-03	15500.6	1027.4
hsa-miR-500a-3p	3.59	3.22E-06	7.00E-05	1275.71	93.06
hsa-miR-380-3p	3.61	2.25E-03	1.44E-02	7.75	0.52
hsa-miR-4470	3.63	1.43E-04	1.69E-03	7.3	0.54
hsa-miR-16-1-3p	3.64	2.99E-05	4.83E-04	19.29	1.38
hsa-miR-1197	3.65	2.07E-03	1.38E-02	7.48	0.44
hsa-miR-18a-3p	3.70	4.71E-05	7.08E-04	110.39	6.98
hsa-miR-376b-3p	3.70	2.09E-04	2.26E-03	10.34	0.67
hsa-miR-655-3p	3.71	6.47E-04	5.57E-03	114.56	7.2
hsa-miR-654-3p	3.71	4.06E-05	6.35E-04	1648.66	99.23
hsa-miR-299-3p	3.74	1.48E-04	1.72E-03	83.87	5.1
hsa-miR-106b-3p	3.75	6.94E-05	9.79E-04	5552.3	359.36
hsa-miR-199b-3p	3.75	3.24E-08	1.42E-06	85137.26	5677.7
hsa-miR-199a-3p	3.75	3.27E-08	1.42E-06	170395.98	11352.78
hsa-miR-6720-3p	3.80	1.15E-06	2.91E-05	25.47	1.59
hsa-miR-1260b	3.80	4.09E-08	1.71E-06	96.14	6.07
hsa-miR-501-3p	3.81	1.93E-06	4.63E-05	718.87	44.66
hsa-miR-542-3p	3.84	3.35E-06	7.00E-05	1512.62	95.88
hsa-miR-424-3p	3.84	9.61E-07	2.58E-05	902.54	55
hsa-miR-369-3p	3.89	3.13E-04	3.24E-03	682.71	34.5
hsa-miR-889-3p	3.91	4.48E-05	6.93E-04	353.08	18.49
hsa-miR-370-3p	3.94	1.12E-04	1.40E-03	2334.68	120.3
hsa-miR-1185-2-3p	3.95	7.85E-05	1.08E-03	27.65	1.45
hsa-miR-216a-3p	3.98	2.19E-03	1.42E-02	2.99	0.18
hsa-miR-323a-3p	4.00	4.53E-06	9.12E-05	219.42	11.36
hsa-miR-214-3p	4.01	9.41E-03	4.28E-02	1.15	0.06
hsa-miR-301b-3p	4.07	9.31E-05	1.22E-03	30.85	1.63
hsa-miR-873-3p	4.08	4.20E-04	4.08E-03	4.14	0.22
hsa-miR-30c-1-3p	4.14	5.62E-07	1.74E-05	237.64	12.08
hsa-miR-188-3p	4.17	6.83E-05	9.75E-04	2.78	0.13
hsa-miR-9-3p	4.18	1.40E-06	3.43E-05	21.06	1.06
hsa-miR-4725-3p	4.25	8.43E-03	3.95E-02	0.72	0.03
hsa-miR-362-3p	4.30	4.80E-06	9.40E-05	43.99	2.01
hsa-miR-487a-3p	4.37	1.02E-05	1.77E-04	79.86	3.13
hsa-miR-135b-3p	4.44	1.00E-07	3.77E-06	42.84	1.82
hsa-miR-433-3p	4.46	1.25E-04	1.52E-03	353.94	12.41
hsa-miR-409-3p	4.49	2.67E-07	8.85E-06	2481.55	89.91
hsa-miR-125a-3p	4.53	7.85E-07	2.21E-05	439.16	17.33
hsa-miR-183-3p	4.63	2.05E-06	4.83E-05	13.24	0.45

hsa-miR-133b	4.65	1.16E-06	2.91E-05	111.81	3.43
hsa-miR-1185-1-3p	4.66	6.40E-06	1.17E-04	123.76	3.86
hsa-miR-892a	4.67	1.44E-04	1.69E-03	5.14	0.19
hsa-miR-3691-3p	4.69	8.08E-03	3.81E-02	0.59	0.01
hsa-miR-1296-3p	4.72	4.13E-03	2.28E-02	0.98	0.03
hsa-miR-493-3p	4.75	4.61E-05	7.03E-04	2704.42	85.74
hsa-miR-6871-3p	4.86	4.60E-03	2.48E-02	1.07	0.03
hsa-miR-181b-3p	4.86	2.07E-10	1.23E-08	111.35	3.5
hsa-miR-496	4.86	5.06E-06	9.52E-05	12.76	0.34
hsa-miR-182-3p	4.87	5.00E-06	9.52E-05	24.24	0.66
hsa-miR-134-3p	4.92	5.88E-06	1.09E-04	13.15	0.37
hsa-miR-1286	4.93	1.52E-04	1.75E-03	2.21	0.07
hsa-miR-99b-3p	5.01	6.89E-13	6.48E-11	7042.46	193
hsa-miR-6889-3p	5.07	5.94E-03	2.96E-02	0.75	0.01
hsa-miR-544a	5.08	1.91E-03	1.31E-02	0.79	0.01
hsa-miR-410-5p	5.08	1.02E-03	8.17E-03	1.2	0.03
hsa-miR-876-3p	5.10	1.85E-04	2.07E-03	2.46	0.07
hsa-miR-10526-3p	5.10	3.59E-03	2.06E-02	0.48	0
hsa-miR-5002-3p	5.15	1.42E-03	1.06E-02	0.81	0.02
hsa-miR-181d-3p	5.18	3.27E-03	1.91E-02	1.24	0.03
hsa-miR-10b-3p	5.27	7.37E-08	2.87E-06	971.58	23.02
hsa-miR-545-3p	5.28	2.74E-03	1.66E-02	0.55	0
hsa-miR-96-3p	5.28	2.74E-03	1.66E-02	1.42	0.03
hsa-miR-892c-3p	5.29	1.48E-03	1.10E-02	1.31	0.03
hsa-miR-504-3p	5.29	4.42E-04	4.26E-03	0.91	0.01
hsa-miR-500b-3p	5.36	4.40E-09	2.26E-07	35.68	0.75
hsa-miR-892b	5.36	1.05E-03	8.32E-03	0.91	0.01
hsa-miR-708-3p	5.36	5.21E-15	5.88E-13	824.88	17.97
hsa-miR-218-2-3p	5.54	1.90E-07	6.52E-06	8.09	0.15
hsa-miR-3167	5.56	1.09E-02	4.83E-02	0.61	0
hsa-miR-7974	5.61	7.14E-06	1.26E-04	5.74	0.1
hsa-let-7a-2-3p	5.64	3.97E-12	2.99E-10	52.75	0.94
hsa-miR-548x-3p	5.75	3.78E-03	2.12E-02	1.17	0.02
hsa-miR-3144-3p	5.77	2.38E-06	5.49E-05	6.88	0.12
hsa-miR-7112-3p	5.77	9.33E-04	7.57E-03	0.75	0
hsa-miR-431-3p	5.77	3.90E-06	8.00E-05	204.34	3.2
hsa-miR-5579-3p	5.79	7.96E-05	1.08E-03	1.27	0.01
hsa-miR-208b-3p	5.84	9.24E-04	7.55E-03	0.95	0
hsa-miR-20a-3p	5.88	7.37E-10	3.96E-08	132.96	2

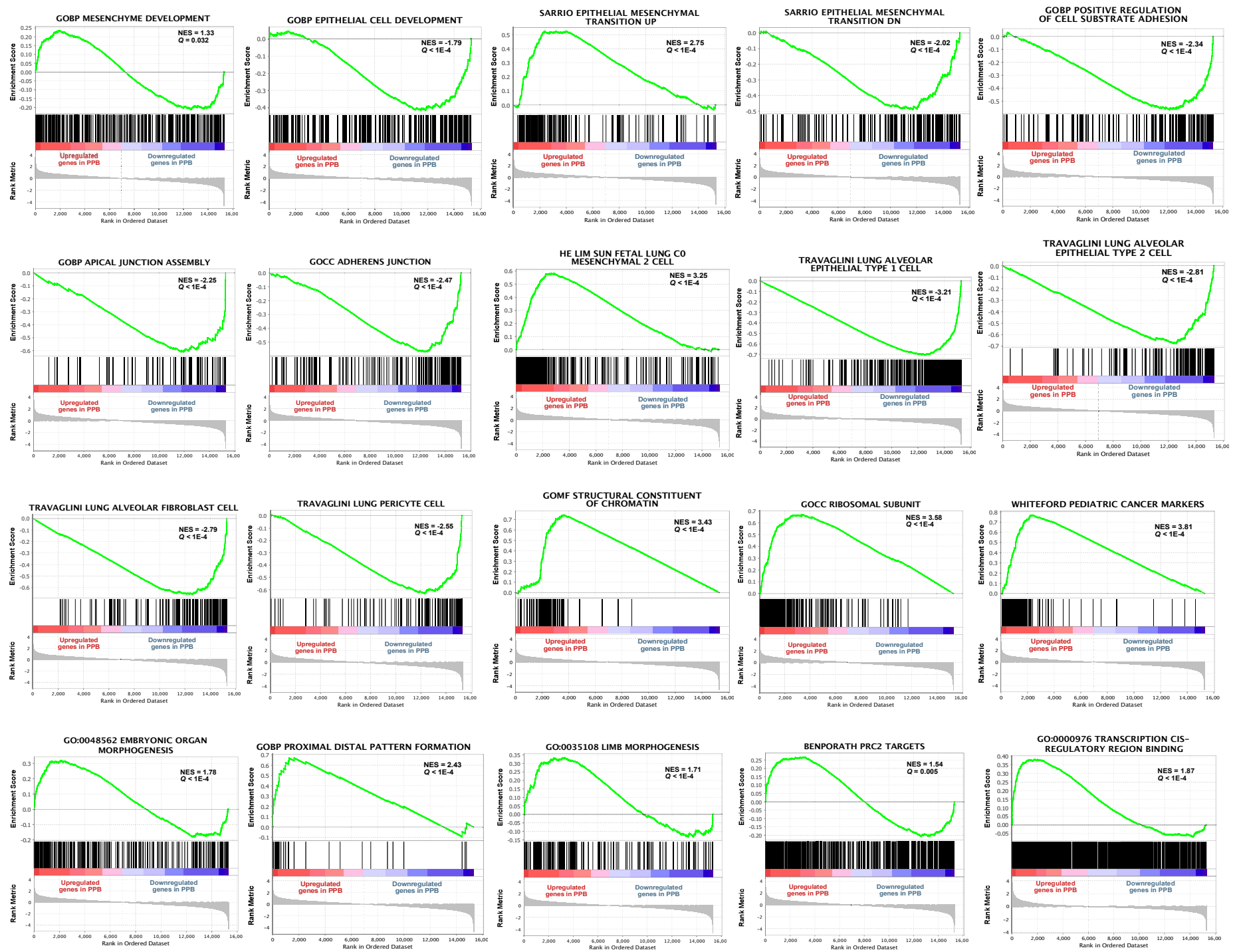
<b>hsa-miR-450a-2-3p</b>	5.94	1.12E-17	2.11E-15	256.09	3.59
<b>hsa-miR-767-3p</b>	6.04	3.45E-05	5.48E-04	1.48	0.02
<b>hsa-miR-483-3p</b>	6.04	4.50E-10	2.54E-08	486.03	6.52
<b>hsa-miR-31-3p</b>	6.05	1.84E-07	6.52E-06	16.11	0.22
<b>hsa-miR-219a-1-3p</b>	6.05	1.13E-12	9.14E-11	107.01	1.46
<b>hsa-miR-6783-3p</b>	6.07	1.22E-04	1.49E-03	2.56	0.04
<b>hsa-miR-597-3p</b>	6.08	8.54E-11	5.67E-09	83.08	1.13
<b>hsa-miR-93-3p</b>	6.23	2.61E-11	1.84E-09	744.12	8.72
<b>hsa-miR-1305</b>	6.25	1.06E-06	2.79E-05	5.3	0.06
<b>hsa-miR-125b-2-3p</b>	6.38	4.54E-18	1.07E-15	8073.45	86.56
<b>hsa-let-7c-3p</b>	6.44	1.61E-22	1.82E-19	311.15	3.1
<b>hsa-miR-181b-2-3p</b>	6.45	1.25E-10	7.83E-09	169.33	1.78
<b>hsa-miR-125b-1-3p</b>	6.48	1.88E-21	1.06E-18	4896.29	47.89
<b>hsa-miR-450b-3p</b>	6.53	7.04E-07	2.04E-05	3.47	0.03
<b>hsa-miR-1247-3p</b>	6.58	1.45E-08	7.09E-07	388.77	3.84
<b>hsa-miR-3118</b>	6.59	5.71E-07	1.74E-05	3.71	0.03
<b>hsa-miR-99a-3p</b>	6.66	1.68E-15	2.11E-13	1326.3	11.9
<b>hsa-miR-100-3p</b>	6.83	8.78E-13	7.62E-11	36.3	0.29
<b>hsa-miR-548a-3p</b>	7.07	6.85E-08	2.76E-06	5.04	0.03
<b>hsa-miR-503-3p</b>	7.16	4.74E-18	1.07E-15	44.89	0.27
<b>hsa-miR-450a-1-3p</b>	7.21	5.01E-21	1.88E-18	232	1.36
<b>hsa-miR-105-3p</b>	7.55	2.50E-08	1.17E-06	4.32	0.02
<b>hsa-miR-206</b>	8.09	7.42E-16	1.20E-13	2971.99	8.81
<b>hsa-miR-135a-3p</b>	10.31	8.59E-16	1.21E-13	175.52	0.13
<b>hsa-miR-196a-3p</b>	10.88	6.65E-15	6.81E-13	26.04	0

## SUPPLEMENTARY FIGURES

## Intensity of SOX2 staining

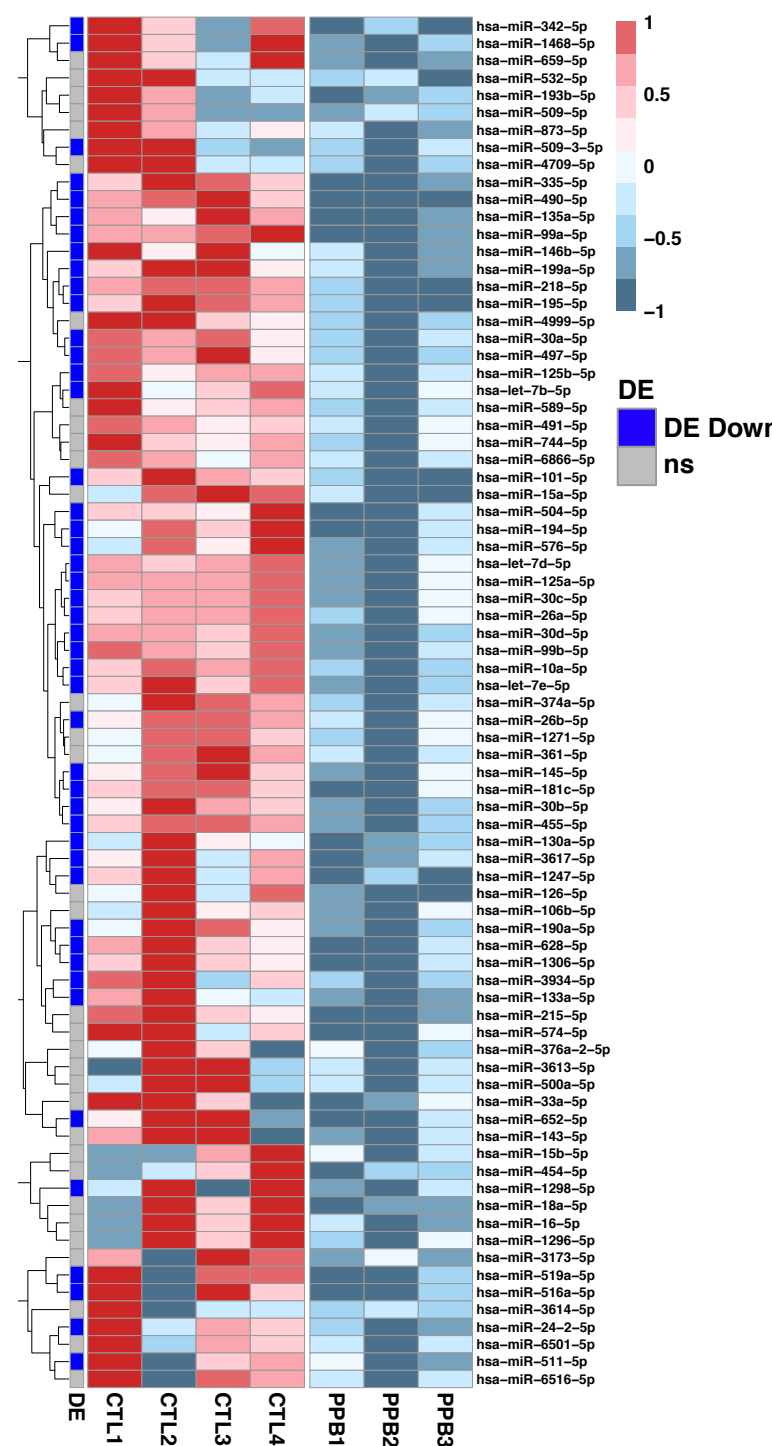


**Figure S1.** Box-and-whisker plot representation of SOX2 fluorescence signal along lung epithelium in control, CPAM  $KRAS^{wt}$  and CPAM  $KRAS^{mut}$  specimens. SOX2 intensity was measured using QuPath. Values represent the average fluorescence intensity per cell along 100  $\mu m$  of epithelium in each specimen. \*  $p$  value < 0.05 (Tukey's multiple comparison test).

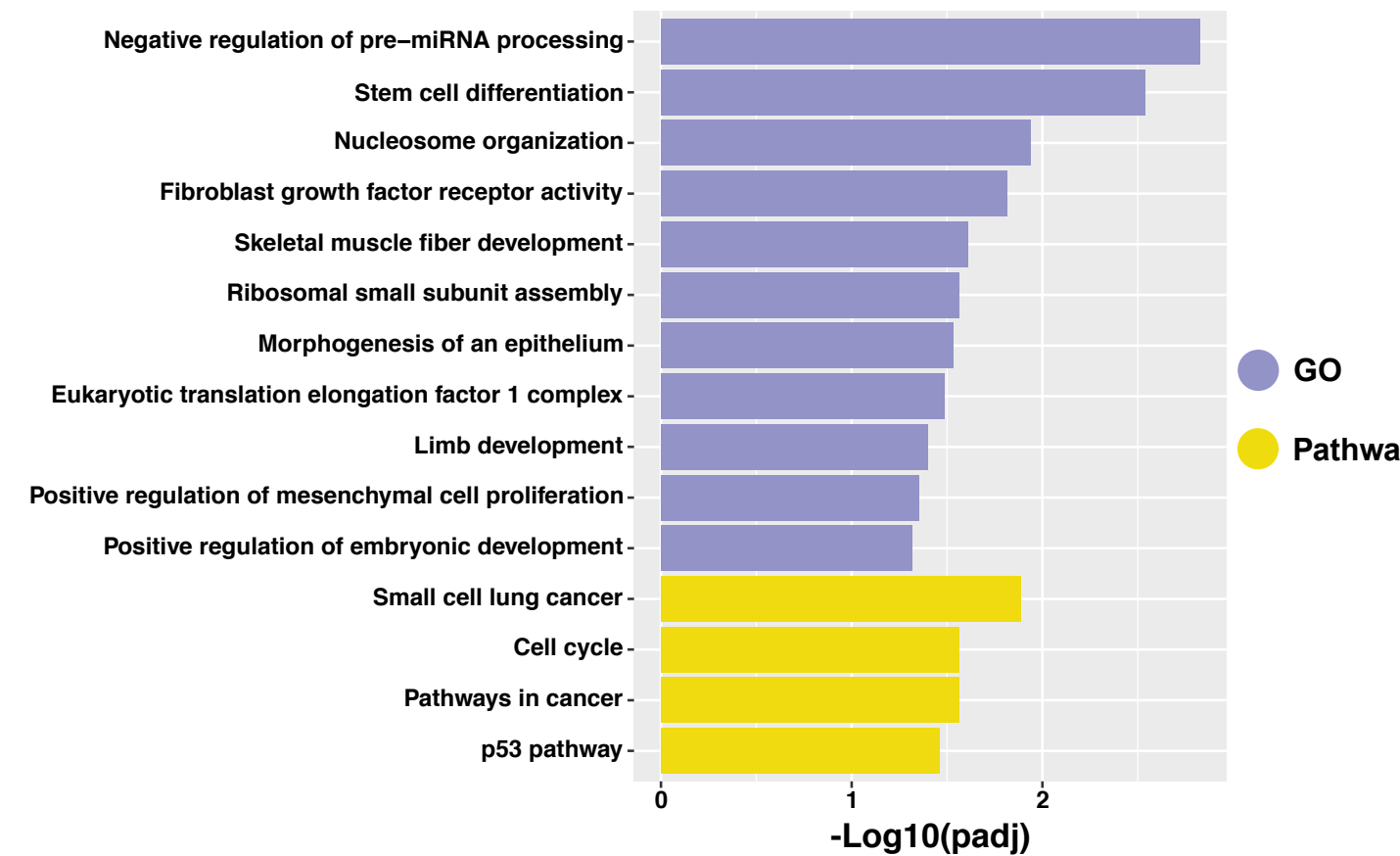


**Figure S2.** Statistically significant enrichment plots of terms associated to GSEA analysis of PPB transcriptome with an FDR-adjusted  $Q < 0.05$  and a  $NES > 1$ . Green curves correspond to the running enrichment score.

**A**



**B**



**Figure S3. (A)** Heatmap and hierarchical clustering of downregulated miRNA-5p common to the three PPB specimens analyzed. They were selected according to a cutoff of the z-score value  $< -0.1$  in all PPB samples. Statistically DE miRNA-5p are shown by blue squares on the left. Data are represented in z-score of the  $\text{Log}_2(\text{mean of RPM} + 1)$ . **(B)** A functional enrichment analysis of downregulated miRNA-5p was performed using microRNA Enrichment Analysis and Annotation (miEAA) with the Over-Representation Analysis (ORA) option surveying across GO (violet) and pathway (yellow) databases. The x-axis corresponds to the  $-\text{Log}_{10}(\text{padj})$ .