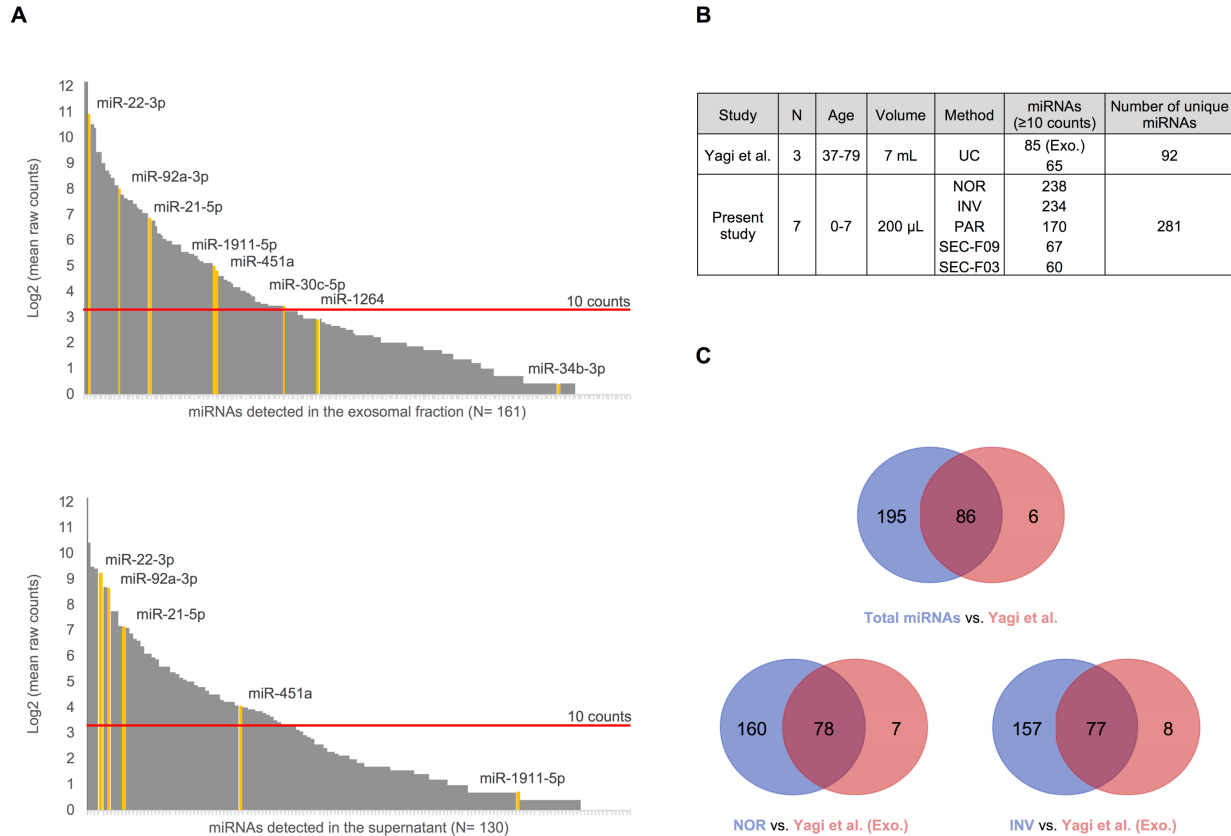
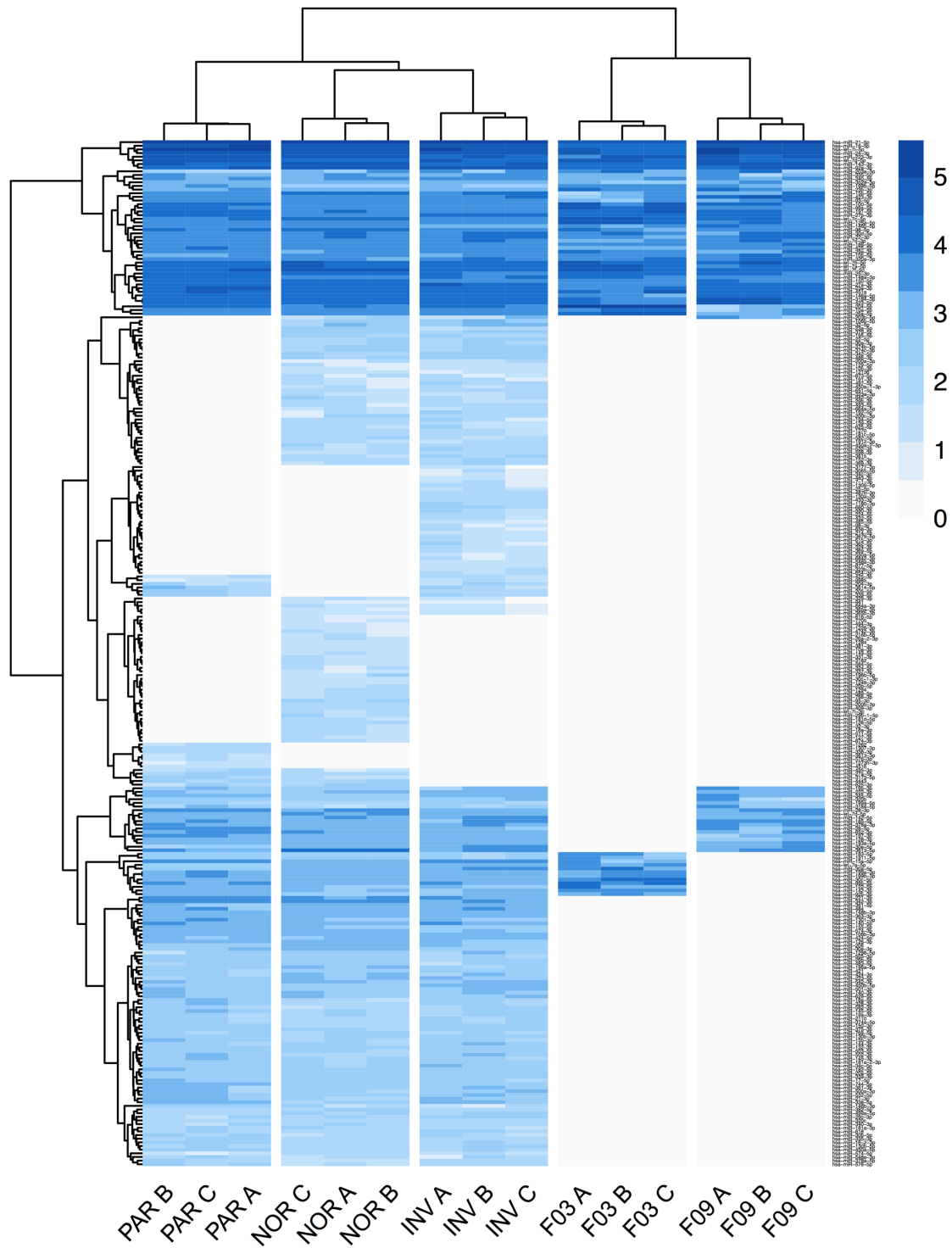


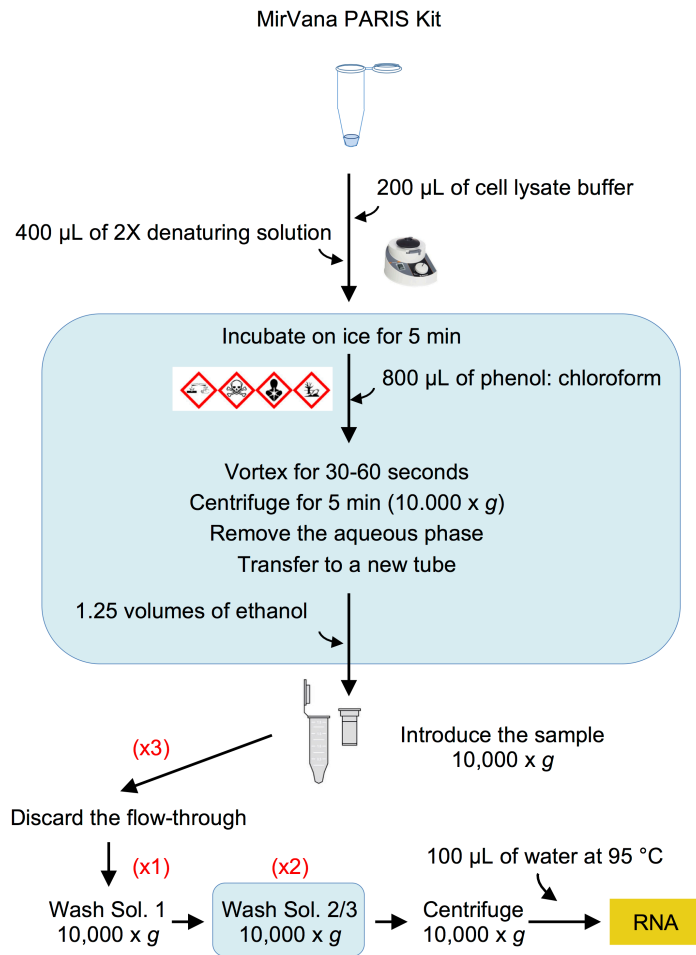
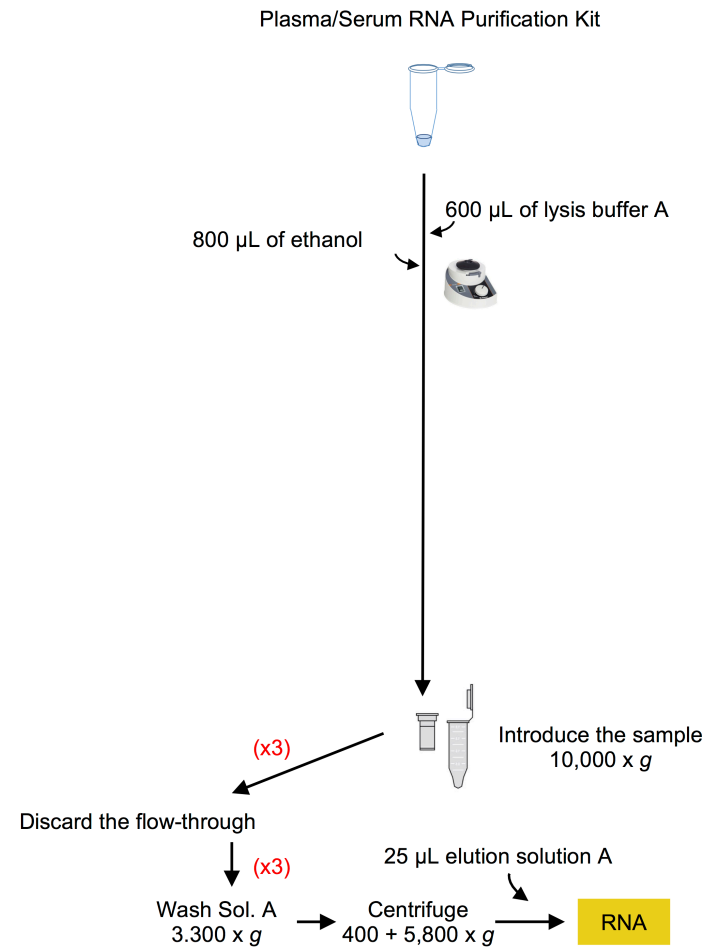
**SUPPLEMENTARY MATERIALS**



**Figure S1.** Comparison of the data obtained here with the results of Yagi et al. [15]. **A**, each miRNA identified detected by Yagi et al. (x-axis) and the number of raw reads on a logarithmic scale (y-axis). Only the eight miRNAs selected as reference miRNAs for this study are highlighted in orange. The horizontal line indicates the threshold chosen to accept a miRNA as detected (10 or more counts). **B**, the summary of the two studies and the number of miRNAs detected by each method. **C**, Venn diagrams showing the number of common miRNAs detected between our study and the one by Yagi et al. in the exosomal fraction (Exo.) (*upper part*), as well as by the NOR and INV protocols in comparison with Yagi et al. (*lower part*). Abbreviations: ultracentrifugation (UC), miRCURY Exosome Isolation Kit from Qiagen (QIA), Total Exosome Isolation Reagent from Invitrogen (INV), miRvana PARIS Kit from Ambion (PAR), and Plasma/Serum RNA Purification Kit from Norgen (NOR).



**Figure S2.** Heatmap representing the abundance of each miRNA for the compared methods. The smallRNAseq counts (10 or more) were TMM-normalized and represented on the logarithmic scale. The darkest blue bars represent the highest abundance and the white bars, the lowest. Each method was assessed in triplicate.

**A****B**

**Figure S3.** Comparison of the two RNA extraction protocols used in this work: **A**, using mirVana PARIS Kit from Ambion and **B**, using the Plasma/Serum RNA Purification Kit from Norgen.

**Table S1.** Results of sequencing and computational post-processing. The green color represents the highest percentage of alignment against the human genome and the red one, the lowest. Abbreviations: mirVana PARIS Kit from Ambion (PAR), Total Exosome Isolation Reagent from Invitrogen (INV), Plasma/Serum RNA Purification Kit from Norgen (NOR), and the fractions 3 (F03) and 9 (F09) of the SEC.

Method	Sample	Total reads	Reads aligned with the genome		Read counts aligned with miRBase22		Average coverage depth	Average length	Average quality	%GC
			N	%	N	%				
DIR	DIR_A	26438319	18470770	69.9	1249070	0.1	104.4	25.8	37.0	52.7
	DIR_B	28440884	18818832	66.2	1392689	0.2	74.7	24.5	37.0	53.0
	DIR_C	30495052	19466510	63.8	1086513	0.2	74.5	23.7	37.0	53.6
F03	F03_A	25958614	9004682	34.7	243519	0.1	60.5	20.2	36.8	55.2
	F03_B	19540619	9312030	47.7	65634	0.2	25.0	18.2	36.8	55.4
	F03_C	25243946	10856518	43.0	84024	0.4	17.2	18.4	36.8	55.7
F09	F09_A	22831445	10171399	44.5	140001	0.2	36.8	18.5	36.8	56.3
	F09_B	24304724	11901408	49.0	121530	0.2	34.4	18.3	36.8	56.0
	F09_C	21646255	10867442	50.2	938047	0.1	87.2	23.1	37.0	53.2
INV	INV_A	27875522	14743858	52.9	1966654	0.3	33.6	18.8	36.8	53.1
	INV_B	22467111	16583184	73.8	6942463	0.2	68.5	21.0	36.9	48.5
	INV_C	26656900	18972809	71.2	7027026	0.2	74.9	20.9	36.9	49.4
NOR	NOR_A	32689429	29545751	90.4	1890229	0.1	267.9	29.5	37.2	50.9
	NOR_B	32771511	25542919	77.9	1511752	0.3	77.9	27.6	37.1	51.1
	NOR_C	34307902	28037677	81.7	1306748	0.2	119.1	28.1	37.1	51.5

**Table S2.** The complete list of the 234 miRNAs detected by smallRNAseq using the INV protocol and their TMM-normalized counts obtained using the INV protocol. The 30 miRNAs that were specifically detected by INV are highlighted in blue and marked with an asterisk (\*). INV\_A, INV\_B, and INV\_C indicate each of the triplicates analyzed.

Name	Normalized counts		
	INV_A	INV_B	INV_C
*hsa-miR-1180-3p	253.22	134.10	57.92
*hsa-miR-660-5p	163.73	174.58	77.13
*hsa-miR-590-3p	206.95	116.67	27.61
*hsa-miR-433-3p	68.14	157.00	97.34
*hsa-miR-130a-3p	82.37	143.61	50.09
*hsa-miR-487b-3p	81.86	60.64	117.12
*hsa-miR-362-5p	197.80	29.67	11.10
*hsa-miR-432-5p	114.92	88.59	30.88
*hsa-miR-224-5p	106.78	53.30	32.87
*hsa-miR-324-3p	135.26	15.12	26.90
*hsa-miR-3065-5p	5.08	150.67	11.67
*hsa-miR-1306-5p	65.09	80.52	11.53
*hsa-miR-25-5p	44.24	78.36	25.33
*hsa-miR-7-1-3p	24.41	111.20	10.67
*hsa-miR-654-3p	60.51	16.85	65.89
*hsa-miR-369-5p	81.86	23.48	25.47
*hsa-miR-323b-3p	20.85	21.17	80.40
*hsa-miR-656-3p	77.80	23.77	7.97
*hsa-miR-3679-5p	58.98	36.44	13.80
*hsa-miR-615-3p	55.42	33.56	13.23
*hsa-miR-6842-3p	63.56	3.60	25.62
*hsa-miR-98-3p	55.93	12.24	20.21
*hsa-miR-214-5p	38.64	31.40	13.52
*hsa-miR-548a-3p	29.49	13.68	33.02
*hsa-miR-877-5p	20.85	27.08	26.18
*hsa-miR-483-3p	21.86	40.62	10.67
*hsa-miR-485-5p	39.15	13.68	9.82
*hsa-miR-34c-3p	12.71	38.46	10.39
*hsa-miR-3177-3p	28.98	23.91	1.57
*hsa-miR-550a-5p	19.32	5.91	27.04
hsa-miR-21-5p	199674.68	305318.16	334780.32
hsa-miR-16-5p	83888.17	61814.95	57789.17
hsa-let-7i-5p	124088.43	35838.43	42205.76
hsa-miR-92a-3p	48643.03	61627.41	51851.52
hsa-miR-24-3p	47785.73	38130.85	60769.24
hsa-miR-143-3p	25078.64	25016.34	34675.98
hsa-miR-27a-3p	35869.55	24684.32	14426.16
hsa-miR-223-3p	19892.16	31949.18	21076.48
hsa-let-7g-5p	39505.17	14256.32	17936.75
hsa-miR-3184-3p	21067.25	16845.03	21471.67
hsa-miR-423-5p	21067.25	16845.03	21471.67
hsa-miR-451a	22932.35	23778.74	12567.76
hsa-let-7f-5p	23255.74	13059.05	21055.85
hsa-let-7b-5p	14439.75	21115.56	21195.17

hsa-miR-23a-3p	20689.96	14972.35	12344.62
hsa-let-7a-5p	11938.04	8124.06	13613.01
hsa-miR-146a-5p	10510.75	12164.13	9982.60
hsa-miR-27b-3p	14672.13	8085.89	8891.81
hsa-miR-204-5p	15340.27	7435.40	7277.19
hsa-miR-30d-5p	5132.58	12326.17	8564.36
hsa-miR-25-3p	13450.26	6155.60	6129.90
hsa-miR-148a-3p	8354.29	6959.49	9244.74
hsa-let-7d-3p	6515.13	9815.54	6892.39
hsa-miR-22-3p	3580.19	8643.04	9894.80
hsa-miR-15b-5p	4621.05	8649.09	8116.81
hsa-miR-423-3p	4454.77	6535.43	8143.27
hsa-miR-191-5p	5827.66	7074.15	5338.96
hsa-miR-29a-3p	5831.22	7083.94	4605.65
hsa-miR-100-5p	6487.67	5880.48	4422.92
hsa-miR-425-5p	4725.28	6760.71	5268.37
hsa-let-7c-5p	5298.85	4772.95	6529.22
hsa-miR-320a-3p	4065.28	8233.25	4122.09
hsa-miR-186-5p	4016.47	7281.85	4393.47
hsa-miR-99a-5p	4990.71	6309.86	3647.63
hsa-miR-93-5p	2654.76	6728.16	5495.64
hsa-miR-340-5p	3294.94	7175.55	3898.24
hsa-miR-3613-5p	1418.14	6751.49	5825.51
hsa-miR-10a-5p	2619.68	5961.57	4675.09
hsa-miR-26a-5p	2845.95	4359.26	4602.80
hsa-miR-125a-5p	3562.90	4977.20	3131.77
hsa-miR-150-5p	3398.67	3884.07	2614.62
hsa-miR-15a-5p	4436.47	2724.11	2389.35
hsa-miR-98-5p	4871.22	2223.56	2362.17
hsa-miR-30e-5p	1246.79	4665.49	3454.80
hsa-miR-10b-5p	1773.57	4260.16	3088.50
hsa-miR-335-5p	1936.79	3350.54	2689.19
hsa-miR-142-5p	1146.11	3511.87	2426.63
hsa-miR-221-3p	2740.70	1723.60	1717.80
hsa-miR-30a-5p	730.68	3307.47	2118.68
hsa-miR-342-3p	1601.20	2396.12	1799.91
hsa-miR-203a-3p	2190.52	527.62	3000.13
hsa-miR-28-3p	1717.13	2031.27	1901.66
hsa-miR-378a-3p	1361.70	2355.65	1633.27
hsa-miR-146b-5p	1647.98	1741.31	1837.33
hsa-miR-484	1101.87	2338.51	1673.11
hsa-miR-185-5p	558.31	2370.77	2111.28
hsa-miR-652-3p	1598.15	1436.23	1524.12
hsa-let-7d-5p	1202.55	1982.44	1369.57
hsa-miR-361-5p	892.89	2061.95	1368.15
hsa-miR-140-5p	2619.17	742.24	742.85
hsa-miR-99b-5p	2129.00	1199.00	714.95
hsa-miR-199a-3p	1661.71	1523.09	806.46
hsa-miR-199b-3p	1654.59	1490.83	812.01
hsa-miR-148b-3p	1471.03	1081.75	1351.92
hsa-miR-363-3p	999.16	1423.41	1155.11
hsa-miR-128-3p	1155.77	1246.24	1146.72
hsa-miR-23b-3p	1624.59	929.50	932.97

hsa-miR-424-5p	894.41	1425.86	921.58
hsa-miR-197-3p	1001.70	1453.95	698.30
hsa-miR-106b-3p	865.94	1377.03	903.51
hsa-miR-450b-5p	652.38	1543.11	949.48
hsa-miR-193a-5p	980.35	1331.66	753.66
hsa-miR-3529-3p	1644.42	718.19	653.48
hsa-miR-30c-5p	1249.33	959.17	733.74
hsa-miR-501-3p	504.92	1320.28	951.04
hsa-miR-28-5p	1299.16	845.52	562.12
hsa-miR-542-3p	496.27	1073.83	993.59
hsa-miR-1301-3p	1697.30	538.86	220.72
hsa-miR-222-3p	752.04	890.89	698.45
hsa-miR-345-5p	743.39	759.82	795.07
hsa-let-7e-5p	698.14	658.41	742.70
hsa-miR-142-3p	520.68	801.01	738.29
hsa-miR-122-5p	1298.14	254.23	505.19
hsa-miR-21-3p	895.94	505.01	553.01
hsa-miR-206	820.17	571.12	556.28
hsa-miR-338-5p	791.19	609.44	520.85
hsa-miR-126-3p	811.53	550.09	536.93
hsa-miR-92b-3p	481.53	664.89	675.25
hsa-miR-361-3p	375.26	871.59	506.47
hsa-miR-19b-3p	132.20	831.69	780.13
hsa-miR-574-3p	305.60	879.66	524.69
hsa-miR-32-5p	280.68	664.61	751.10
hsa-miR-320b	432.21	356.07	785.25
hsa-miR-223-5p	723.06	443.50	395.47
hsa-miR-30e-3p	567.46	441.77	528.25
hsa-miR-199b-5p	806.45	400.72	292.44
hsa-miR-34c-5p	726.61	532.95	234.81
hsa-miR-106b-5p	252.21	667.77	515.72
hsa-miR-144-3p	502.38	620.53	255.30
hsa-miR-500a-3p	227.29	525.17	601.25
hsa-miR-629-5p	357.97	361.98	629.28
hsa-miR-421	418.99	390.21	528.82
hsa-miR-1298-5p	136.27	796.69	394.19
hsa-miR-424-3p	147.46	591.86	529.24
hsa-miR-502-3p	259.32	594.17	325.88
hsa-miR-532-5p	312.71	581.35	278.50
hsa-miR-140-3p	187.12	603.53	320.62
hsa-miR-181a-2-3p	492.72	357.51	219.58
hsa-miR-486-3p	563.39	293.70	187.42
hsa-miR-203b-5p	15.25	13.54	1003.41
hsa-miR-155-5p	348.31	366.87	256.87
hsa-miR-3184-5p	555.26	155.28	222.00
hsa-miR-483-5p	38.64	483.11	377.54
hsa-miR-199a-5p	514.07	222.69	162.09
hsa-miR-182-5p	402.21	169.39	311.23
hsa-miR-150-3p	230.34	193.74	416.82
hsa-miR-339-3p	270.51	211.02	356.77
hsa-miR-145-3p	451.53	236.80	138.61
hsa-miR-20a-5p	326.44	205.98	287.03
hsa-miR-29c-3p	238.98	284.19	266.83

hsa-miR-17-5p	399.16	280.88	95.20
hsa-miR-26b-5p	60.00	363.27	349.51
hsa-miR-769-5p	148.48	467.70	155.54
hsa-miR-582-3p	126.10	437.74	207.06
hsa-miR-499a-5p	156.61	256.83	348.80
hsa-miR-132-3p	269.49	261.72	226.98
hsa-miR-503-5p	175.42	340.95	226.41
hsa-miR-328-3p	186.61	373.21	147.43
hsa-miR-15b-3p	372.21	163.05	131.21
hsa-miR-145-5p	68.14	342.24	254.30
hsa-miR-744-5p	227.80	252.22	184.43
hsa-miR-196a-5p	170.85	116.53	373.70
hsa-miR-375-3p	240.51	200.65	202.50
hsa-miR-195-5p	489.16	50.27	54.08
hsa-miR-130b-3p	228.82	192.01	165.93
hsa-miR-342-5p	208.48	167.95	191.55
hsa-miR-339-5p	335.60	149.37	81.54
hsa-miR-3615	175.93	158.45	217.02
hsa-miR-374b-5p	160.17	218.94	168.78
hsa-miR-374c-3p	160.17	218.94	168.78
hsa-miR-183-5p	228.31	150.67	165.22
hsa-miR-1911-5p	167.29	159.02	191.12
hsa-miR-19a-3p	54.92	244.15	216.31
hsa-miR-505-3p	87.46	326.11	85.53
hsa-miR-18a-5p	213.56	170.83	112.00
hsa-miR-30a-3p	140.34	243.29	104.45
hsa-miR-2110	220.68	96.65	169.49
hsa-miR-374a-5p	212.04	78.21	193.40
hsa-miR-22-5p	100.17	185.67	196.81
hsa-miR-532-3p	267.97	127.62	81.40
hsa-miR-369-3p	104.24	262.30	107.30
hsa-miR-130b-5p	105.76	188.55	164.93
hsa-miR-618	175.42	216.93	55.93
hsa-miR-450a-5p	69.15	223.26	151.70
hsa-miR-16-2-3p	108.81	181.20	153.12
hsa-miR-379-5p	69.66	165.79	166.50
hsa-miR-30b-5p	213.05	157.29	31.45
hsa-miR-382-5p	111.36	145.34	133.91
hsa-miR-497-5p	173.39	107.02	63.33
hsa-miR-192-5p	163.22	118.40	58.63
hsa-miR-152-3p	109.32	166.37	58.49
hsa-miR-204-3p	43.73	178.32	100.90
hsa-miR-320c	107.29	90.60	124.95
hsa-miR-3614-5p	194.24	97.66	29.32
hsa-miR-200c-3p	47.80	121.71	147.15
hsa-miR-194-5p	212.54	96.51	6.12
hsa-miR-205-5p	160.17	71.59	79.55
hsa-miR-598-3p	129.66	52.72	115.13
hsa-miR-651-5p	111.36	62.37	104.88
hsa-miR-340-3p	74.75	99.39	102.60
hsa-miR-378a-5p	132.71	50.99	76.56
hsa-miR-450a-1-3p	117.97	25.78	114.56
hsa-miR-548e-3p	9.66	170.11	73.72



hsa-miR-181a-3p	138.81	81.96	31.31
hsa-miR-335-3p	133.22	50.70	67.74
hsa-miR-664a-5p	17.29	106.73	124.38
hsa-miR-625-5p	169.83	36.73	38.42
hsa-miR-450a-2-3p	71.19	99.53	72.58
hsa-miR-23a-5p	33.05	78.21	119.11
hsa-miR-582-5p	69.15	44.65	110.72
hsa-miR-191-3p	146.44	53.73	12.38
hsa-miR-1912-3p	26.95	106.16	55.64
hsa-miR-576-5p	52.88	67.41	59.20
hsa-miR-323a-3p	42.71	33.42	91.65
hsa-miR-942-5p	60.00	21.32	85.67
hsa-miR-181c-5p	62.54	63.38	38.42
hsa-miR-493-5p	61.02	46.67	49.38
hsa-miR-200a-3p	19.83	35.00	97.20
hsa-miR-1270	67.12	59.06	21.77
hsa-miR-29b-3p	80.34	37.02	29.03
hsa-miR-9985	40.68	63.23	40.13
hsa-miR-574-5p	30.51	64.53	41.41
hsa-miR-425-3p	46.27	51.13	38.57
hsa-miR-139-5p	49.83	36.30	12.95
hsa-miR-873-5p	60.00	9.22	29.03
hsa-miR-129-5p	16.78	38.89	35.86
hsa-miR-146b-3p	28.47	4.03	52.94
hsa-miR-12136	8.64	42.49	27.61
hsa-miR-329-3p	32.03	31.98	3.42
hsa-miR-10b-3p	16.78	30.10	16.79
hsa-miR-365b-3p	17.80	28.23	5.83
hsa-miR-365a-3p	19.32	24.49	6.12
hsa-miR-664a-3p	18.31	21.89	9.39
hsa-miR-941	11.69	9.65	3.42

**Table S3.** The complete list of the miRNAs isolated by each method. Abbreviations: mirVana PARIS Kit from Ambion (PAR), Total Exosome Isolation Reagent from Invitrogen (INV), Plasma/Serum RNA Purification Kit from Norgen (NOR), and the fractions 3 (F03) and 9 (F09) of the SEC.

Methods	Common miRNAs	miRNAs
F03 F09 INV NOR PAR	48	hsa-miR-30d-5p hsa-let-7i-5p hsa-miR-23b-3p hsa-miR-23a-3p hsa-miR-143-3p hsa-miR-125a-5p hsa-miR-10b-5p hsa-miR-423-3p hsa-miR-146a-5p hsa-miR-10a-5p hsa-miR-99a-5p hsa-miR-146b-5p hsa-miR-24-3p hsa-miR-15b-5p hsa-miR-223-3p hsa-miR-451a hsa-miR-150-5p hsa-miR-199b-5p hsa-let-7b-5p hsa-let-7f-5p hsa-miR-335-5p hsa-miR-26a-5p hsa-miR-186-5p hsa-miR-93-5p hsa-let-7a-5p hsa-miR-92a-3p hsa-let-7c-5p hsa-miR-203a-3p hsa-miR-340-5p hsa-miR-148a-3p hsa-miR-25-3p hsa-miR-204-5p hsa-miR-423-5p hsa-miR-425-5p hsa-miR-98-5p hsa-miR-3184-3p hsa-miR-29a-3p hsa-let-7g-5p hsa-miR-27b-3p hsa-miR-21-5p hsa-let-7d-3p hsa-miR-3529-3p hsa-miR-100-5p hsa-miR-22-3p hsa-miR-16-5p hsa-miR-320a-3p hsa-miR-27a-3p hsa-miR-191-5p
F03 INV NOR PAR	12	hsa-miR-92b-3p hsa-miR-99b-5p hsa-let-7e-5p hsa-miR-199a-3p hsa-miR-30c-5p hsa-miR-30a-5p hsa-miR-199b-3p hsa-miR-122-5p hsa-miR-183-5p hsa-miR-15a-5p hsa-miR-1911-5p hsa-miR-142-3p
F09 INV NOR PAR	18	hsa-miR-185-5p hsa-miR-652-3p hsa-miR-3613-5p hsa-miR-193a-5p hsa-miR-28-3p hsa-miR-378a-3p hsa-miR-142-5p hsa-miR-28-5p hsa-miR-128-3p hsa-miR-345-5p hsa-miR-19b-3p hsa-miR-199a-5p hsa-let-7d-5p hsa-miR-30e-5p hsa-miR-320b hsa-miR-197-3p hsa-miR-3184-5p hsa-miR-222-3p
INV NOR PAR	74	hsa-miR-140-5p hsa-miR-361-5p hsa-miR-1298-5p hsa-miR-502-3p hsa-miR-30e-3p hsa-miR-34c-5p hsa-miR-221-3p hsa-miR-375-3p hsa-miR-17-5p hsa-miR-542-3p hsa-miR-181a-2-3p hsa-miR-335-3p hsa-miR-450a-5p hsa-miR-18a-5p hsa-miR-2110 hsa-miR-374a-5p hsa-miR-450b-5p hsa-miR-744-5p hsa-miR-196a-5p hsa-miR-150-3p hsa-miR-424-5p hsa-miR-363-3p hsa-miR-30b-5p hsa-miR-320c hsa-miR-424-3p hsa-miR-629-5p hsa-miR-340-3p hsa-miR-126-3p hsa-miR-361-3p hsa-miR-146b-3p hsa-miR-182-5p hsa-miR-769-5p hsa-miR-19a-3p hsa-miR-15b-3p hsa-miR-1301-3p hsa-miR-574-3p hsa-miR-145-3p hsa-miR-342-3p hsa-miR-29c-3p hsa-miR-483-5p hsa-miR-181a-3p hsa-miR-144-3p hsa-miR-499a-5p hsa-miR-16-2-3p hsa-miR-339-3p hsa-miR-576-5p hsa-miR-338-5p hsa-miR-130b-5p hsa-miR-618 hsa-miR-130b-3p hsa-miR-421 hsa-miR-206 hsa-miR-382-5p hsa-miR-582-3p hsa-miR-106b-3p hsa-miR-501-3p hsa-miR-574-5p hsa-miR-548e-3p hsa-miR-223-5p hsa-miR-140-3p hsa-miR-505-3p hsa-miR-484 hsa-miR-26b-5p hsa-miR-132-3p hsa-miR-155-5p hsa-miR-532-5p hsa-miR-378a-5p hsa-miR-145-5p hsa-miR-20a-5p hsa-miR-21-3p hsa-miR-148b-3p hsa-miR-500a-3p hsa-miR-503-5p hsa-miR-328-3p
F09 INV NOR	1	hsa-miR-203b-5p
INV PAR	6	hsa-miR-3614-5p hsa-miR-425-3p hsa-miR-205-5p hsa-miR-339-5p hsa-miR-9985 hsa-miR-204-3p
NOR PAR	5	hsa-miR-27a-5p hsa-miR-3173-5p hsa-miR-4443 hsa-miR-625-3p hsa-miR-495-3p

INV NOR	45	hsa-miR-3615 hsa-miR-873-5p hsa-miR-374b-5p hsa-miR-450a-2-3p hsa-miR-1270 hsa-miR-195-5p hsa-miR-1912-3p hsa-miR-532-3p hsa-miR-497-5p hsa-miR-194-5p hsa-miR-651-5p hsa-miR-493-5p hsa-miR-598-3p hsa-miR-22-5p hsa-miR-139-5p hsa-miR-486-3p hsa-miR-941 hsa-miR-323a-3p hsa-miR-129-5p hsa-miR-342-5p hsa-miR-191-3p hsa-miR-450a-1-3p hsa-miR-32-5p hsa-miR-23a-5p hsa-miR-329-3p hsa-miR-664a-5p hsa-miR-374c-3p hsa-miR-582-5p hsa-miR-192-5p hsa-miR-10b-3p hsa-miR-29b-3p hsa-miR-200c-3p hsa-miR-12136 hsa-miR-30a-3p hsa-miR-942-5p hsa-miR-181c-5p hsa-miR-200a-3p hsa-miR-106b-5p hsa-miR-379-5p hsa-miR-625-5p hsa-miR-369-3p hsa-miR-365b-3p hsa-miR-664a-3p hsa-miR-365a-3p hsa-miR-152-3p
PAR	7	hsa-miR-576-3p hsa-miR-1262 hsa-miR-3613-3p hsa-miR-1307-3p hsa-miR-4516 hsa-miR-338-3p hsa-miR-1273h-3p
INV	30	hsa-miR-656-3p hsa-miR-654-3p hsa-miR-98-3p hsa-miR-1306-5p hsa-miR-7-1-3p hsa-miR-483-3p hsa-miR-25-5p hsa-miR-6842-3p hsa-miR-548a-3p hsa-miR-487b-3p hsa-miR-877-5p hsa-miR-3679-5p hsa-miR-224-5p hsa-miR-550a-5p hsa-miR-369-5p hsa-miR-615-3p hsa-miR-485-5p hsa-miR-660-5p hsa-miR-324-3p hsa-miR-3065-5p hsa-miR-323b-3p hsa-miR-362-5p hsa-miR-432-5p hsa-miR-130a-3p hsa-miR-590-3p hsa-miR-1180-3p hsa-miR-214-5p hsa-miR-433-3p hsa-miR-34c-3p hsa-miR-3177-3p
NOR	35	hsa-miR-149-5p hsa-miR-381-3p hsa-miR-30c-1-3p hsa-miR-589-5p hsa-miR-216b-5p hsa-miR-1226-3p hsa-miR-127-3p hsa-miR-324-5p hsa-miR-1294 hsa-miR-7705 hsa-miR-3182 hsa-miR-26a-2-3p hsa-miR-126-5p hsa-miR-4742-3p hsa-miR-494-3p hsa-miR-181d-5p hsa-miR-766-3p hsa-miR-616-5p hsa-miR-10a-3p hsa-let-7i-3p hsa-miR-1284 hsa-miR-196b-5p hsa-miR-584-5p hsa-miR-32-3p hsa-miR-18a-3p hsa-miR-200b-3p hsa-miR-337-3p hsa-miR-874-3p hsa-miR-331-3p hsa-miR-20b-5p hsa-miR-409-3p hsa-miR-1249-3p hsa-miR-29b-1-5p hsa-miR-95-3p hsa-miR-511-5p
F03	0	
F09	0	

**Table S4.** The complete list of the pathways predicted by ConsensusPathDB considering the 9,952 target genes of the 281 miRNAs detected in our study by smallRNAseq.

Pathway name	Set size	Candidates contained	p-value	q-value	Pathway source
Axon guidance	358	276 (77.1%)	2.83e-23	6.48e-20	Reactome
Membrane Trafficking	582	414 (71.1%)	5.05e-22	5.78e-19	Reactome
Vesicle-mediated transport	620	434 (70.0%)	7.36e-21	5.62e-18	Reactome
Endocytosis - Homo sapiens (human)	244	189 (77.5%)	1.06e-16	6.06e-14	KEGG
Axon guidance - Homo sapiens (human)	175	143 (81.7%)	1.46e-16	6.7e-14	KEGG
Pathways in cancer - Homo sapiens (human)	526	362 (68.8%)	9.5e-16	3.63e-13	KEGG
Developmental Biology	620	418 (67.4%)	1.12e-15	3.67e-13	Reactome
Signaling by Receptor Tyrosine Kinases	423	299 (70.7%)	1.37e-15	3.92e-13	Reactome
Proteoglycans in cancer - Homo sapiens (human)	201	154 (76.6%)	3.81e-13	8.9e-11	KEGG
Disease	510	344 (67.5%)	3.88e-13	8.9e-11	Reactome
MAPK signaling pathway - Homo sapiens (human)	295	213 (72.2%)	6.11e-13	1.27e-10	KEGG
Intracellular signaling by second messengers	245	177 (72.2%)	5.14e-11	9.76e-09	Reactome
Neuronal System	368	252 (68.5%)	5.54e-11	9.76e-09	Reactome
Protein-protein interactions at synapses	88	74 (84.1%)	2.35e-10	3.84e-08	Reactome
Diseases of signal transduction	248	177 (71.4%)	2.64e-10	4.03e-08	Reactome
Cellular senescence - Homo sapiens (human)	160	121 (75.6%)	5.52e-10	7.9e-08	KEGG
Hippo signaling pathway - Homo sapiens (human)	154	117 (76.0%)	6.49e-10	8.75e-08	KEGG
Signaling pathways regulating pluripotency of stem cells - Homo sapiens (human)	139	106 (76.3%)	2.85e-09	3.63e-07	KEGG
Adherens junction - Homo sapiens (human)	72	61 (84.7%)	5.03e-09	6.07e-07	KEGG
Insulin signaling pathway - Homo sapiens (human)	137	104 (75.9%)	6.24e-09	7.15e-07	KEGG
PIP3 activates AKT signaling	214	152 (71.0%)	8.26e-09	9.01e-07	Reactome
Bacterial invasion of epithelial cells - Homo sapiens (human)	74	62 (83.8%)	9.28e-09	9.41e-07	KEGG
Breast cancer - Homo sapiens (human)	147	110 (74.8%)	9.44e-09	9.41e-07	KEGG
Thyroid hormone signaling pathway - Homo sapiens (human)	116	90 (77.6%)	1,00E-08	9.57e-07	KEGG
Wnt signaling pathway - Homo sapiens (human)	149	111 (74.5%)	1.24e-08	1.14e-06	KEGG
Intra-Golgi and retrograde Golgi-to-ER traffic	186	134 (72.0%)	1.51e-08	1.33e-06	Reactome

Signaling by TGF-beta family members	96	76 (79.2%)	2.94e-08	2.49e-06	Reactome
cAMP signaling pathway - Homo sapiens (human)	199	141 (70.9%)	3.66e-08	2.89e-06	KEGG
Focal adhesion - Homo sapiens (human)	199	141 (70.9%)	3.66e-08	2.89e-06	KEGG
Human papillomavirus infection - Homo sapiens (human)	339	225 (66.4%)	3.98e-08	3.02e-06	KEGG
Ras signaling pathway - Homo sapiens (human)	232	161 (69.4%)	4.09e-08	3.02e-06	KEGG
FoxO signaling pathway - Homo sapiens (human)	132	99 (75.0%)	4.24e-08	3.04e-06	KEGG
Regulation of actin cytoskeleton - Homo sapiens (human)	213	149 (70.0%)	5.79e-08	4.02e-06	KEGG
Signaling by VEGF	100	78 (78.0%)	6.38e-08	4.3e-06	Reactome
MAPK family signaling cascades	237	163 (68.8%)	8.82e-08	5.78e-06	Reactome
Clathrin-mediated endocytosis	138	102 (73.9%)	9.56e-08	6,00E-06	Reactome
Phospholipase D signaling pathway - Homo sapiens (human)	146	107 (73.3%)	9.87e-08	6,00E-06	KEGG
Cushing syndrome - Homo sapiens (human)	154	112 (72.7%)	9.94e-08	6,00E-06	KEGG
Rap1 signaling pathway - Homo sapiens (human)	206	144 (69.9%)	1.03e-07	6.08e-06	KEGG
Insulin resistance - Homo sapiens (human)	107	82 (76.6%)	1.21e-07	6.92e-06	KEGG
Melanogenesis - Homo sapiens (human)	101	78 (77.2%)	1.38e-07	7.69e-06	KEGG
cGMP-PKG signaling pathway - Homo sapiens (human)	163	117 (71.8%)	1.7e-07	9.24e-06	KEGG
EPH-Ephrin signaling	74	60 (81.1%)	1.75e-07	9.24e-06	Reactome
Netrin-1 signaling	41	37 (90.2%)	1.8e-07	9.24e-06	Reactome
Extracellular matrix organization	294	196 (66.7%)	1.81e-07	9.24e-06	Reactome
L1CAM interactions	103	79 (76.7%)	1.93e-07	9.62e-06	Reactome
Rho GTPase cycle	144	105 (72.9%)	2,00E-07	9.74e-06	Reactome
Gastric cancer - Homo sapiens (human)	149	108 (72.5%)	2.23e-07	1.05e-05	KEGG
Death Receptor Signalling	141	103 (73.0%)	2.24e-07	1.05e-05	Reactome
Signaling by TGF-beta Receptor Complex	67	55 (82.1%)	2.6e-07	1.19e-05	Reactome
Chronic myeloid leukemia - Homo sapiens (human)	76	61 (80.3%)	2.78e-07	1.25e-05	KEGG
Phosphatidylinositol signaling system - Homo sapiens (human)	99	76 (76.8%)	3.08e-07	1.36e-05	KEGG
VEGFA-VEGFR2 Pathway	92	71 (77.2%)	5.26e-07	2.27e-05	Reactome
Parathyroid hormone synthesis, secretion and action - Homo sapiens (human)	106	80 (75.5%)	5.34e-07	2.27e-05	KEGG
Signaling by NTRKs	89	69 (77.5%)	5.58e-07	2.33e-05	Reactome
Colorectal cancer - Homo sapiens (human)	86	67 (77.9%)	5.88e-07	2.41e-05	KEGG
Transport of small molecules	666	407 (61.1%)	7.3e-07	2.93e-05	Reactome

Antigen processing: Ubiquitination & Proteasome degradation	264	176 (66.7%)	7.6e-07	3.00E-05	Reactome
ErbB signaling pathway - Homo sapiens (human)	85	66 (77.6%)	8.9e-07	3.46e-05	KEGG
AGE-RAGE signaling pathway in diabetic complications - Homo sapiens (human)	99	75 (75.8%)	9.32e-07	3.56e-05	KEGG
Signaling by PDGF	54	45 (83.3%)	1.43e-06	5.39e-05	Reactome
mapkinase signaling pathway	57	47 (82.5%)	1.53e-06	5.58e-05	BioCarta
Neurexins and neuroligins	57	47 (82.5%)	1.53e-06	5.58e-05	Reactome
Glioma - Homo sapiens (human)	71	56 (78.9%)	2.46e-06	8.81e-05	KEGG
NCAM signaling for neurite out-growth	59	48 (81.4%)	2.54e-06	8.93e-05	Reactome
Regulation of PTEN gene transcription	62	50 (80.6%)	2.57e-06	8.93e-05	Reactome
Choline metabolism in cancer - Homo sapiens (human)	99	74 (74.7%)	2.67e-06	9.14e-05	KEGG
PTEN Regulation	96	72 (75.0%)	2.94e-06	9.92e-05	Reactome
AMPK signaling pathway - Homo sapiens (human)	120	87 (72.5%)	3.25e-06	0.000108	KEGG
PI3K-Akt signaling pathway - Homo sapiens (human)	354	226 (63.8%)	3.37e-06	0.00011	KEGG
Signaling by NTRK1 (TRKA)	76	59 (77.6%)	3.42e-06	0.00011	Reactome
Translocation of GLUT4 to the plasma membrane	32	29 (90.6%)	3.47e-06	0.00011	Reactome
Ephrin signaling	19	19 (100.0%)	3.96e-06	0.000124	Reactome
Class I MHC mediated antigen processing & presentation	324	208 (64.2%)	4.73e-06	0.000146	Reactome
Metabolism of carbohydrates	264	173 (65.5%)	4.82e-06	0.000147	Reactome
HIF-1 signaling pathway - Homo sapiens (human)	100	74 (74.0%)	5.06e-06	0.000153	KEGG
G alpha (12/13) signalling events	89	67 (75.3%)	5.18e-06	0.000154	Reactome
Oxytocin signaling pathway - Homo sapiens (human)	152	106 (69.7%)	5.79e-06	0.00017	KEGG
Transmission across Chemical Synapses	224	149 (66.5%)	6.34e-06	0.000181	Reactome
Hepatitis B - Homo sapiens (human)	144	101 (70.1%)	6.39e-06	0.000181	KEGG
Adrenergic signaling in cardiomyocytes - Homo sapiens (human)	144	101 (70.1%)	6.39e-06	0.000181	KEGG
p75 NTR receptor-mediated signalling	99	73 (73.7%)	7.28e-06	0.000203	Reactome
Autophagy - animal - Homo sapiens (human)	128	91 (71.1%)	7.51e-06	0.000207	KEGG
TGF-beta signaling pathway - Homo sapiens (human)	85	64 (75.3%)	8.33e-06	0.000227	KEGG
MAPK1/MAPK3 signaling	203	136 (67.0%)	9.07e-06	0.000241	Reactome
Endocrine and other factor-regulated calcium reabsorption - Homo sapiens (human)	47	39 (83.0%)	9.08e-06	0.000241	KEGG
Central carbon metabolism in cancer - Homo sapiens (human)	65	51 (78.5%)	9.15e-06	0.000241	KEGG
Transport to the Golgi and subsequent modification	168	115 (68.5%)	9.62e-06	0.000248	Reactome

keratinocyte differentiation	53	43 (81.1%)	9.8e-06	0.000248	BioCarta
Synthesis of PIPs at the plasma membrane	53	43 (81.1%)	9.8e-06	0.000248	Reactome
Golgi Associated Vesicle Biogenesis	56	45 (80.4%)	9.85e-06	0.000248	Reactome
Activation of BH3-only proteins	30	27 (90.0%)	1.06e-05	0.000262	Reactome
mcalpain and friends in cell motility	30	27 (90.0%)	1.06e-05	0.000262	BioCarta
Neurotrophin signaling pathway - Homo sapiens (human)	119	85 (71.4%)	1.11e-05	0.000267	KEGG
Glycosaminoglycan metabolism	119	85 (71.4%)	1.11e-05	0.000267	Reactome
Apelin signaling pathway - Homo sapiens (human)	137	96 (70.1%)	1.15e-05	0.000274	KEGG
Glycogen metabolism	22	21 (95.5%)	1.19e-05	0.00028	Reactome
RAF/MAP kinase cascade	197	132 (67.0%)	1.21e-05	0.000283	Reactome
Golgi-to-ER retrograde transport	116	83 (71.6%)	1.26e-05	0.000292	Reactome
Signaling by EGFR	43	36 (83.7%)	1.36e-05	0.000313	Reactome
Semaphorin interactions	64	50 (78.1%)	1.39e-05	0.000317	Reactome
role of egf receptor transactivation by gpcrs in cardiac hypertrophy	33	29 (87.9%)	1.43e-05	0.000322	BioCarta
Prostate cancer - Homo sapiens (human)	97	71 (73.2%)	1.49e-05	0.000332	KEGG
Endometrial cancer - Homo sapiens (human)	58	46 (79.3%)	1.51e-05	0.000332	KEGG
Pancreatic cancer - Homo sapiens (human)	75	57 (76.0%)	1.59e-05	0.000348	KEGG
TNF signaling pathway - Homo sapiens (human)	110	79 (71.8%)	1.62e-05	0.000351	KEGG
mTOR signaling pathway - Homo sapiens (human)	151	104 (68.9%)	1.68e-05	0.000359	KEGG
Clathrin derived vesicle budding	72	55 (76.4%)	1.73e-05	0.000363	Reactome
trans-Golgi Network Vesicle Budding	72	55 (76.4%)	1.73e-05	0.000363	Reactome
Transcriptional Regulation by TP53	374	234 (62.6%)	1.86e-05	0.000388	Reactome
Cargo recognition for clathrin-mediated endocytosis	99	72 (72.7%)	1.88e-05	0.000389	Reactome
C-type lectin receptor signaling pathway - Homo sapiens (human)	104	75 (72.1%)	2.09e-05	0.000427	KEGG
Protein processing in endoplasmic reticulum - Homo sapiens (human)	165	112 (67.9%)	2.26e-05	0.000458	KEGG
Post-translational protein modification	1383	791 (57.2%)	2.33e-05	0.000468	Reactome
Opioid Signalling	82	61 (74.4%)	2.58e-05	0.000514	Reactome
Regulation of TP53 Activity	162	110 (67.9%)	2.6e-05	0.000514	Reactome
Cell-Cell communication	124	87 (70.2%)	2.7e-05	0.000528	Reactome
Collagen biosynthesis and modifying enzymes	68	52 (76.5%)	2.78e-05	0.00054	Reactome
Glucagon signaling pathway - Homo sapiens (human)	103	74 (71.8%)	2.93e-05	0.00056	KEGG

Circadian Clock	35	30 (85.7%)	2.93e-05	0.00056	Reactome
PI Metabolism	84	62 (73.8%)	3.35e-05	0.000634	Reactome
Beta-catenin independent WNT signaling	92	67 (72.8%)	3.39e-05	0.000637	Reactome
sprouty regulation of tyrosine kinase signals	20	19 (95.0%)	4.02e-05	0.000748	BioCarta
Long-term potentiation - Homo sapiens (human)	67	51 (76.1%)	4.13e-05	0.000764	KEGG
Transcriptional regulation by RUNX2	75	56 (74.7%)	4.6e-05	0.000837	Reactome
Gastric acid secretion - Homo sapiens (human)	75	56 (74.7%)	4.6e-05	0.000837	KEGG
Fc gamma R-mediated phagocytosis - Homo sapiens (human)	91	66 (72.5%)	4.81e-05	0.000868	KEGG
Thyroid cancer - Homo sapiens (human)	37	31 (83.8%)	5.42e-05	0.000957	KEGG
RHO GTPases Activate WASPs and WAVES	37	31 (83.8%)	5.42e-05	0.000957	Reactome
Gap junction - Homo sapiens (human)	88	64 (72.7%)	5.43e-05	0.000957	KEGG
Calcium signaling pathway - Homo sapiens (human)	186	123 (66.1%)	5.93e-05	0.00103	KEGG
Intrinsic Pathway for Apoptosis	43	35 (81.4%)	5.94e-05	0.00103	Reactome
Infectious disease	253	162 (64.0%)	6.3e-05	0.00109	Reactome
bioactive peptide induced signaling pathway	33	28 (84.8%)	8.06e-05	0.00138	BioCarta
Collagen formation	92	66 (71.7%)	8.4e-05	0.00143	Reactome
TP53 Regulates Transcription of Cell Cycle Genes	51	40 (78.4%)	8.72e-05	0.00147	Reactome
MAP kinase activation	65	49 (75.4%)	9.02e-05	0.0015	Reactome
Interleukin-17 signaling	65	49 (75.4%)	9.02e-05	0.0015	Reactome
Signaling by NOTCH	120	83 (69.2%)	9.19e-05	0.00152	Reactome
Human cytomegalovirus infection - Homo sapiens (human)	225	145 (64.4%)	9.51e-05	0.00155	KEGG
links between pyk2 and map kinases	26	23 (88.5%)	9.55e-05	0.00155	BioCarta
Longevity regulating pathway - multiple species - Homo sapiens (human)	62	47 (75.8%)	9.88e-05	0.00159	KEGG