

Supplement to “False discovery rate control: Moving beyond the Benjamini–Hochberg method”

S1 Missingness

Supplementary Figure S2.1 presents a bar plot displaying the number of missing pairs of miRNAs for each patient. Figure S2.1 shows that the number of missing miRNA pairs can range from 12 to 232 across the eighteen patients. Only two patients exhibit more than 100 missing pairs, while the majority—70% of the patients—have fewer than 50 missing pairs. On the other hand, Figure S2.2 presents a histogram showcasing the distribution of the missing miRNA pairs. This histogram indicates that a significant proportion—approximately 59.77%—of the miRNAs possess at least one pair of missing observations. However, most of these miRNAs (about 48.76% of them) have at most two missing pairs of observations. Nevertheless, there are fifteen miRNAs with 50% missing observations each. Table S1 lists the miRNAs detected using the imputed data. Moreover, many of the additional discoveries correspond to miRNAs with moderate to severe missingness (cf. Table S1), hinting that these discoveries may result from imputation-driven variance deflation.

Table S1. Significantly deregulated miRNAs with the median-imputed data. Table of the significantly deregulated miRNAs detected using the median imputed data. These miRNAs were detected by at least one of the following four methods at the level of significance 0.05: BH, SABHA, TST-GBH, and LSL-GBH. (The last two methods are shown in the table as TST and LSL, respectively.) The columns “Chr.” and “strand” indicate which chromosome and strand the miRNA belongs to, respectively. The column $\Delta\Delta Ct$ gives the $\Delta\Delta Ct$ values for each miRNA. We report the raw p-values before the FDR correction because the GBH methods, e.g., TST-GBH, LSL-GBH, and SABHA, do not yield FDR-corrected p-values. The signs after the p-values indicate whether the miRNAs were upregulated ($\uparrow$), or downregulated ($\downarrow$). The column “Missing pairs” gives the number of missing pairs of observations for each miRNA. The column “Significant tests” indicates which methods detected the miRNA to be significantly deregulated.

$\dagger$ These miRNAs did not appear in Table 1, which is based on the non-imputed data. We have thirteen such miRNAs in total. Note that these miRNAs also have a relatively higher amount of missingness.

MiRNA	chr.	strand	$\Delta\Delta Ct$	p-value	Missing pairs	Significant tests
hsa-miR-548k $\dagger$	chr11	+	-2.7	$3.86E^{-05}$ ($\uparrow$)	8	BH, TST, SABHA
hsa-miR-1293	chr12	-	-4.8	$1.51E^{-06}$ ($\uparrow$)	9	BH, TST, SABHA
hsa-miR-7-5p	chr15	+	-3.1	$2.8E^{-04}$ ($\uparrow$)	2	all tests
hsa-miR-133a-3p	chr18	-	6.7	$5.32E^{-05}$ ($\downarrow$)	0	all tests
hsa-miR-1	chr18	-	5.2	$9.38E^{-04}$ ($\downarrow$)	0	all tests
hsa-miR-206	chr6	+	6.0	$1.97E^{-04}$ ($\downarrow$)	0	BH, TST, SABHA
hsa-miR-133b $\dagger$	chr6	+	2.7	$6.80E^{-04}$ ($\downarrow$)	8	BH, TST, SABHA
hsa-miR-31-3p	chr9	-	-3.8	$2.00E^{-05}$ ($\uparrow$)	2	all tests
hsa-miR-31-5p	chr9	-	3.4	$6.18E^{-04}$ ($\uparrow$)	0	all tests
hsa-miR-204-5p	chr9	-	4.6	$2.19E^{-04}$ ($\downarrow$)	2	BH, TST, SABHA
hsa-miR-504-5p $\dagger$	chrX	-	4.7	$6.00E^{-04}$ ($\downarrow$)	6	all tests
hsa-miR-891a-5p $\dagger$	chrX	-	4.4	$2.84E^{-04}$ ($\downarrow$)	7	all tests
hsa-miR-508-3p $\dagger$	chrX	-	4.0	$7.91E^{-04}$ ($\downarrow$)	6	all tests
hsa-miR-1290 $\dagger$	chr1	-	-2.2	$3.45E^{-03}$ ($\uparrow$)	2	TST
hsa-miR-135b-3p $\dagger$	chr1	-	-2.2	$2.42E^{-03}$ ($\uparrow$)	2	TST
hsa-miR-200b-5p $\dagger$	chr1	+	-3.5	$2.66E^{-03}$ ($\uparrow$)	3	TST
hsa-miR-200c-5p $\dagger$	chr12	+	-2.3	$5.31E^{-03}$ ($\uparrow$)	3	TST
hsa-miR-1247-5p	chr14	-	2.4	$4.40E^{-03}$ ($\downarrow$)	2	TST, LSL
hsa-miR-211-5p $\dagger$	chr15	-	3.7	$4.90E^{-03}$ ($\downarrow$)	4	TST, LSL
hsa-miR-147b	chr15	+	-2.1	$2.96E^{-03}$ ($\uparrow$)	2	TST, LSL
hsa-miR-21-5p	chr17	+	-2.2	$3.66E^{-03}$ ($\uparrow$)	0	TST
hsa-miR-99a-3p	chr21	+	2.8	$5.83E^{-03}$ ($\downarrow$)	0	TST, LSL
hsa-miR-383-5p $\dagger$	chr8	-	2.7	$3.05E^{-02}$ ($\downarrow$)	4	TST
hsa-miR-486-3p	chr8	-	2.4	$2.81E^{-03}$ ($\downarrow$)	0	TST, LSL
hsa-miR-486-5p	chr8	-	2.0	$1.78E^{-02}$ ($\downarrow$)	0	TST
hsa-miR-770-5p $\dagger$	chr14	+	3.0	$3.71E^{-03}$ ($\downarrow$)	3	LSL
hsa-miR-299-5p $\dagger$	chr14	+	2.5	$3.62E^{-03}$ ($\downarrow$)	4	LSL

S2 Figures on missingness.

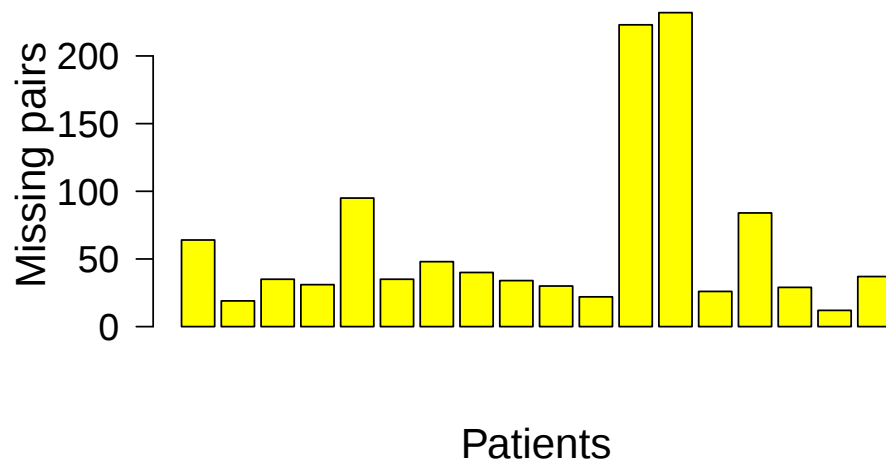


Fig S2.1. Barplot of the number of missing pairs of miRNAs across patients. Here the number of patients is 18, and the total number of miRNAs is 522. The x-axis corresponds to the patients, and the y-axis corresponds to the number of missing pairs of miRNAs corresponding to each patient. Each patient had at least twelve missing pairs of miRNA expressions.

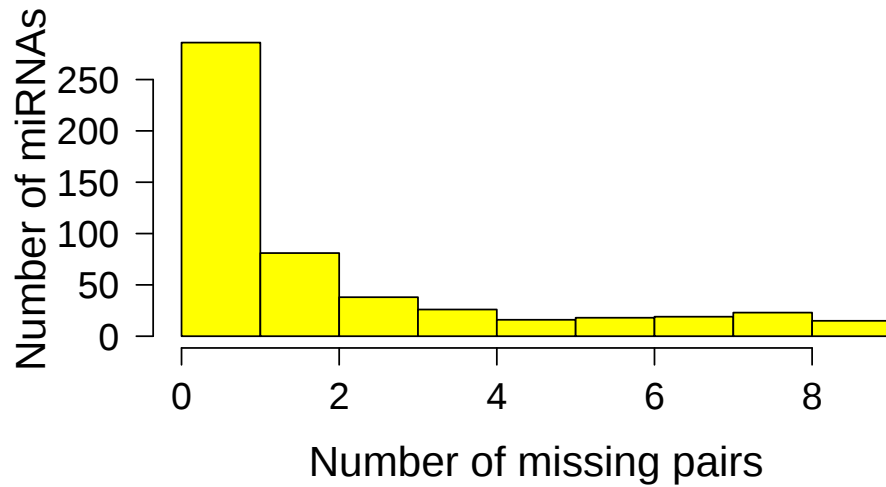


Fig S2.2. Histogram of the number of missing pairs of miRNAs. Here we considered the 522 miRNAs from our analysis. The x-axis corresponds to the number of missing pairs, and the y-axis corresponds to the number of miRNAs with that many missing pairs.

S3 Table of group sizes

Table S2. Table of group sizes. This table lists the size, chromosome number, and the corresponding strand for each group. Here size corresponds to the number of miRNAs in a group. There can be at most two groups on the same strand of the same chromosome because there are only two arms, each of which corresponds to a different group.

Group number	Size	Chr.	Strand
1	9	chr1	-
2	19	chr1	-
3	10	chr1	+
4	3	chr1	+
5	2	chr10	-
6	4	chr10	-
7	2	chr10	+
8	4	chr10	+
9	4	chr11	-
10	11	chr11	-
11	6	chr11	+
12	8	chr12	-
13	5	chr12	+
14	8	chr12	+
15	5	chr13	-
16	13	chr13	+
17	4	chr14	-
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Group number	Size	Chr.	Strand
18	55	chr14	+
19	9	chr15	-
20	7	chr15	+
21	2	chr16	-
22	5	chr16	+
23	3	chr16	+
24	13	chr17	-
25	17	chr17	-
26	2	chr17	+
27	5	chr17	+
28	3	chr18	-
29	8	chr19	-
30	3	chr19	-
31	5	chr19	+
32	37	chr19	+
33	3	chr2	-
34	3	chr2	-
35	8	chr2	+
36	3	chr20	-
37	7	chr20	+
38	6	chr21	+
39	4	chr22	-
40	10	chr22	+
41	8	chr3	-
42	2	chr3	-
43	4	chr3	+
44	10	chr3	+
45	3	chr4	-
46	6	chr4	-
47	4	chr4	+
48	5	chr4	+
49	2	chr5	-
50	9	chr5	-
51	7	chr5	+
52	4	chr6	-
53	2	chr6	+
54	6	chr7	-
55	17	chr7	-
56	2	chr7	+
57	7	chr7	+
58	5	chr8	-
59	8	chr8	-
60	3	chr8	+
61	3	chr9	-
62	4	chr9	-
63	14	chr9	+
64	6	chrX	-
65	32	chrX	-
66	9	chrX	+
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Group number	Size	Chr.	Strand
67	5	chrX	+