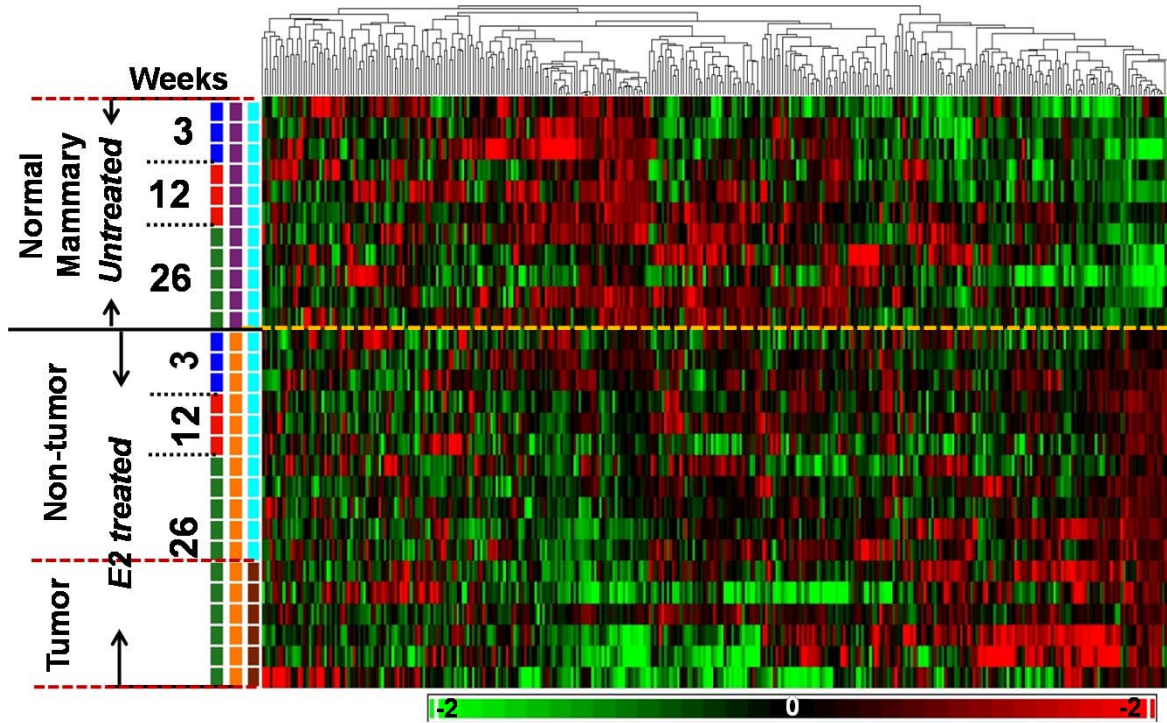


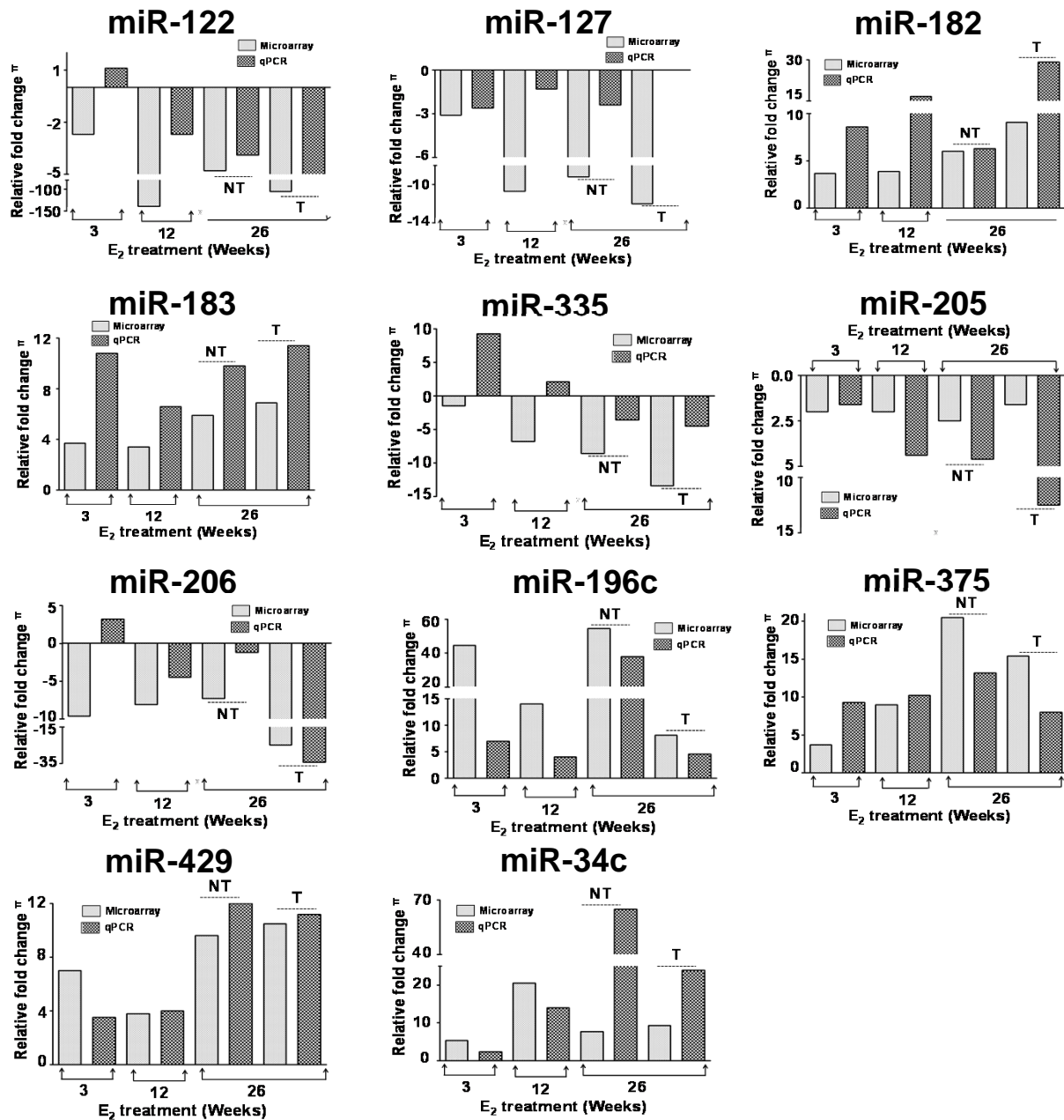
# Supplementary Fig. S1



**Figure S1:** Hierarchical clustering of 28 samples and 351 miRNAs. Rows represent sample, and columns represent miRNA. The bar code at the bottom represents the color scales of the log<sub>2</sub> values

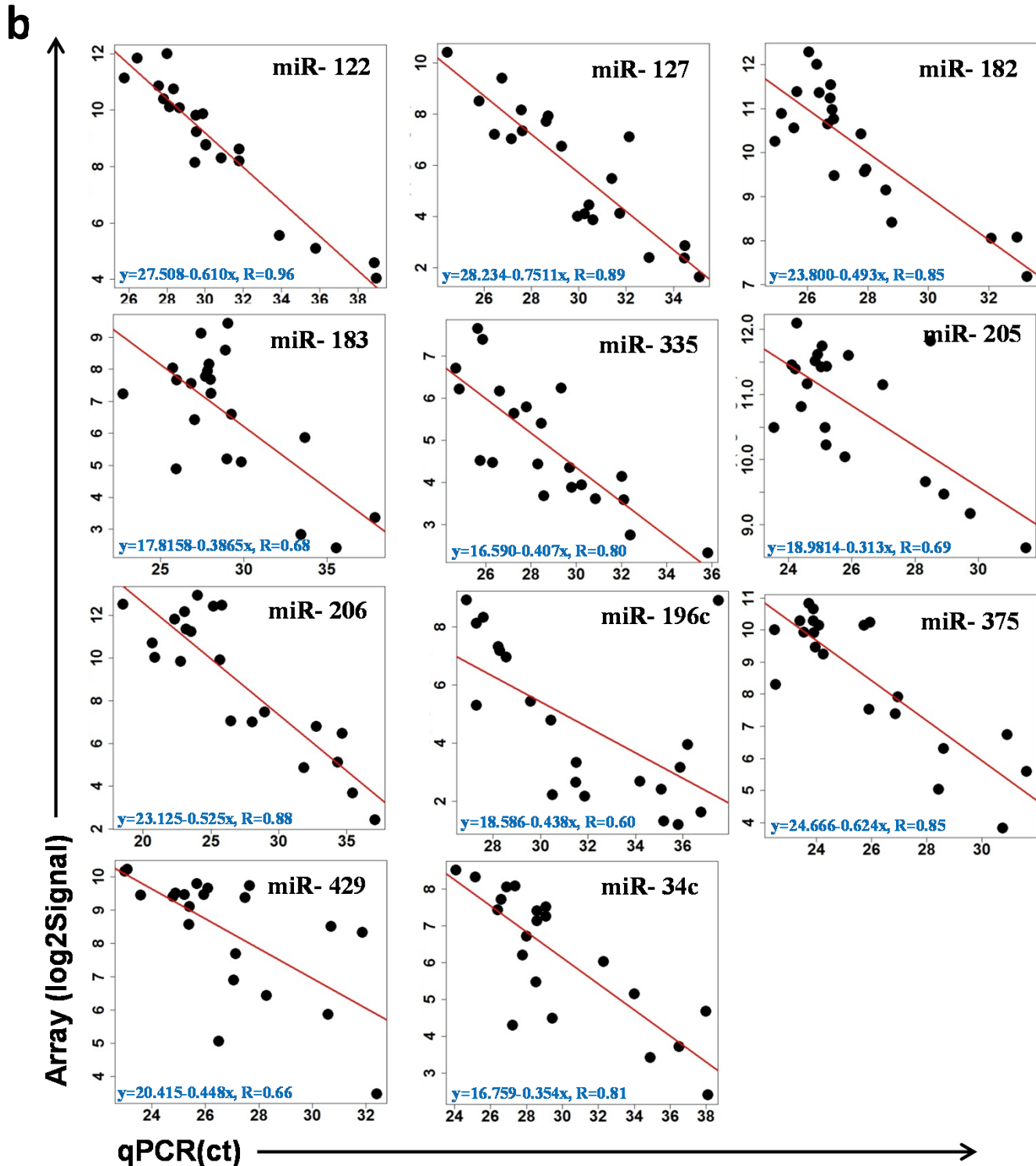
# Supplementary Fig S2

a



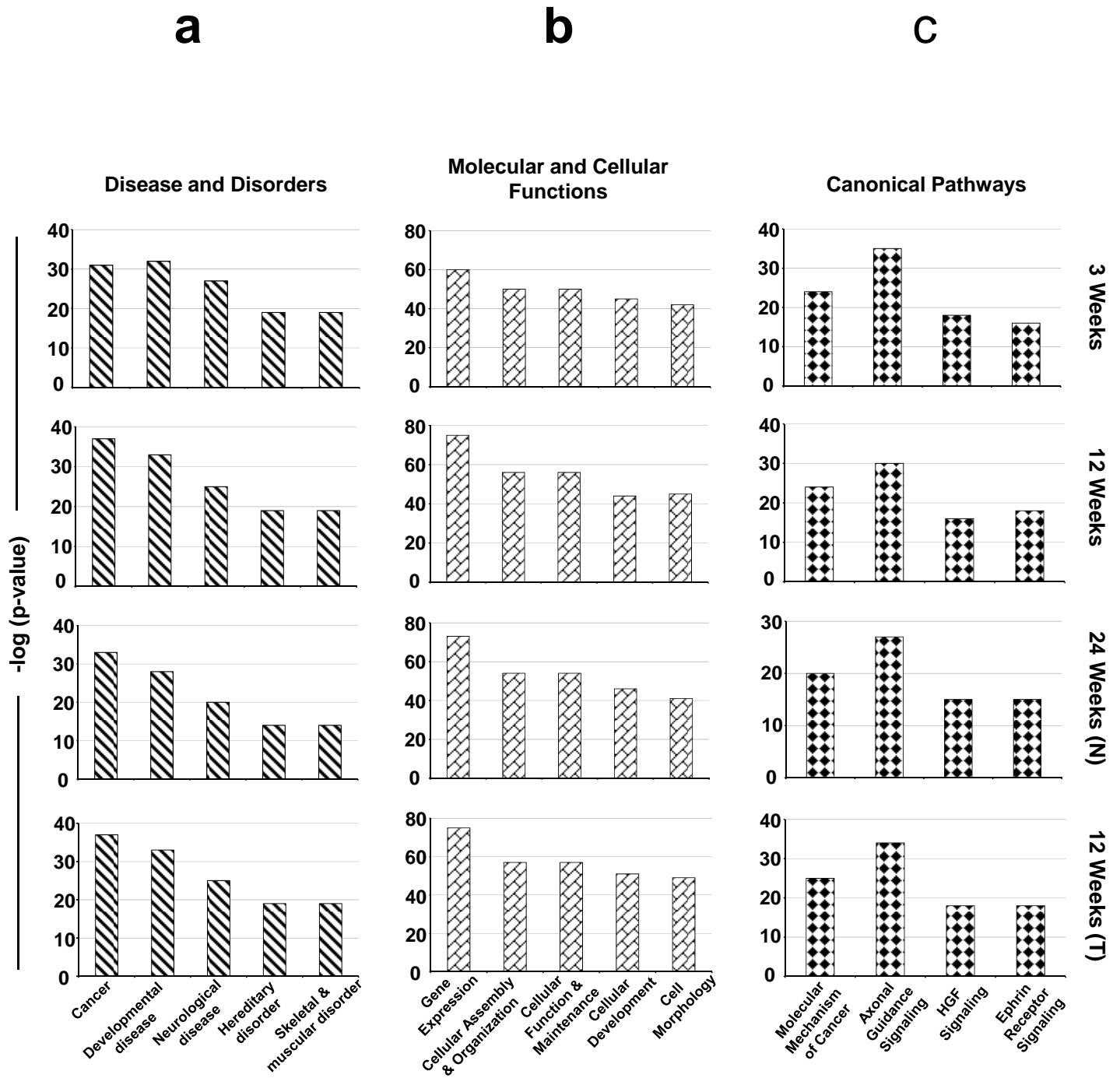
**Figure S2a:** miRNAs were analyzed by qRT-PCR in mammary and tumor tissues of  $E_2$ -alone and EA-treated ACI rats. Data represents mean fold change in mRNA expression relative to the untreated control of five animals each. NT represents non-tumor (distal normal mammary) and T represents tumor tissue.

# Supplementary Fig S2



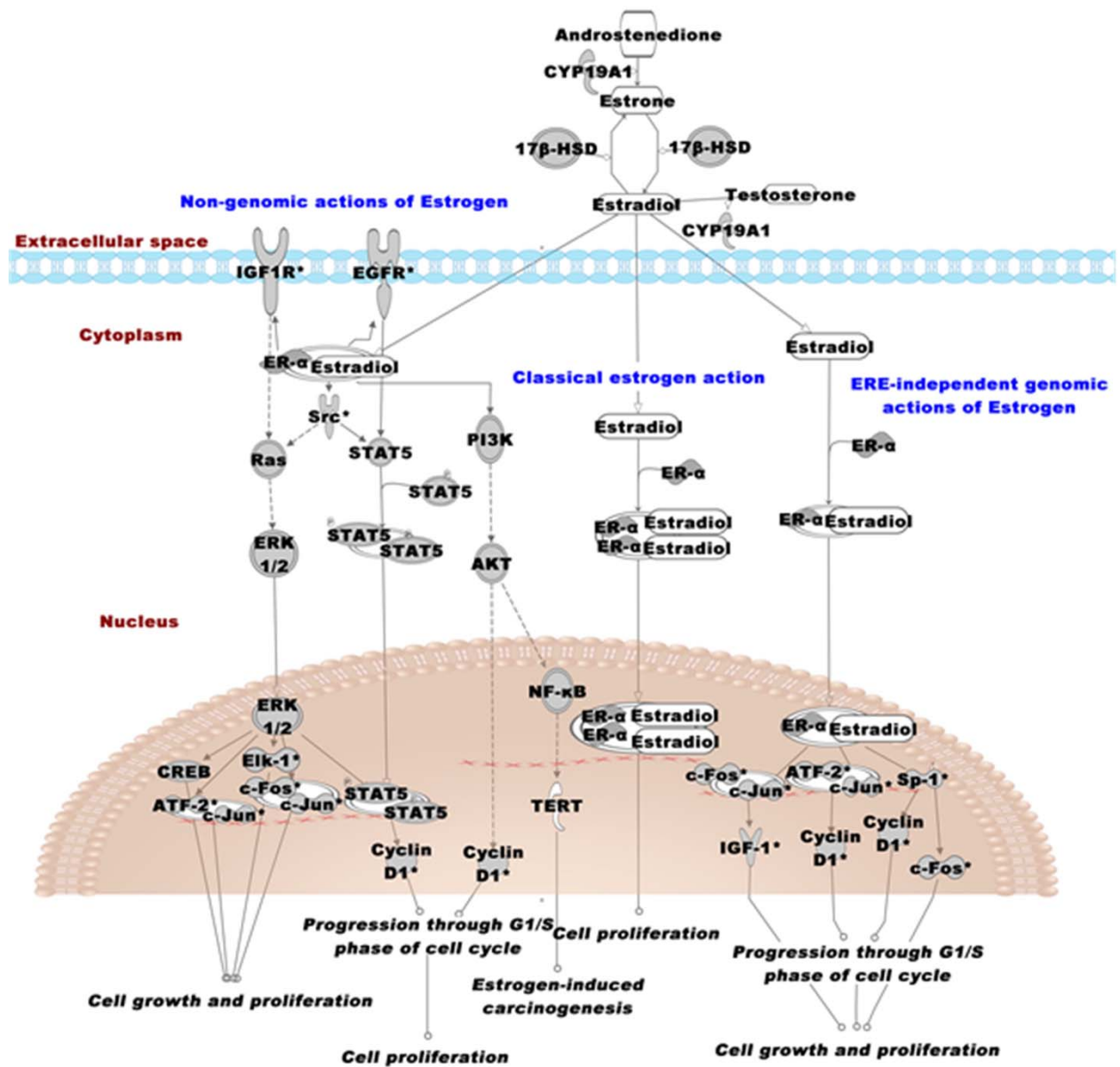
**Figure S2b:** Correlation analysis of the qPCR and microarray results were compared by plotting the qPCR cycle threshold (Ct) value versus the log<sub>2</sub> of the array signal for each miRNA at 3, 12 and 26 week. The correlation between the two methods was 0.96-0.60

# Supplementary Fig. S3



**Figure S3:** Ingenuity Pathway Analysis (IPA) software was used to determine the related functions and pathways of the miRNA target genes identified by TargetScan, a) top 5 diseases and disorders, b) top 5 molecular and cellular functions and c) top 4 canonical pathways.

# Supplementary Fig.S4



**Figure S4:** An overlay of predicted targets from 26 week tumor tissue on E<sub>2</sub>-mediated breast cancer pathways

# Supplementary Fig. S5

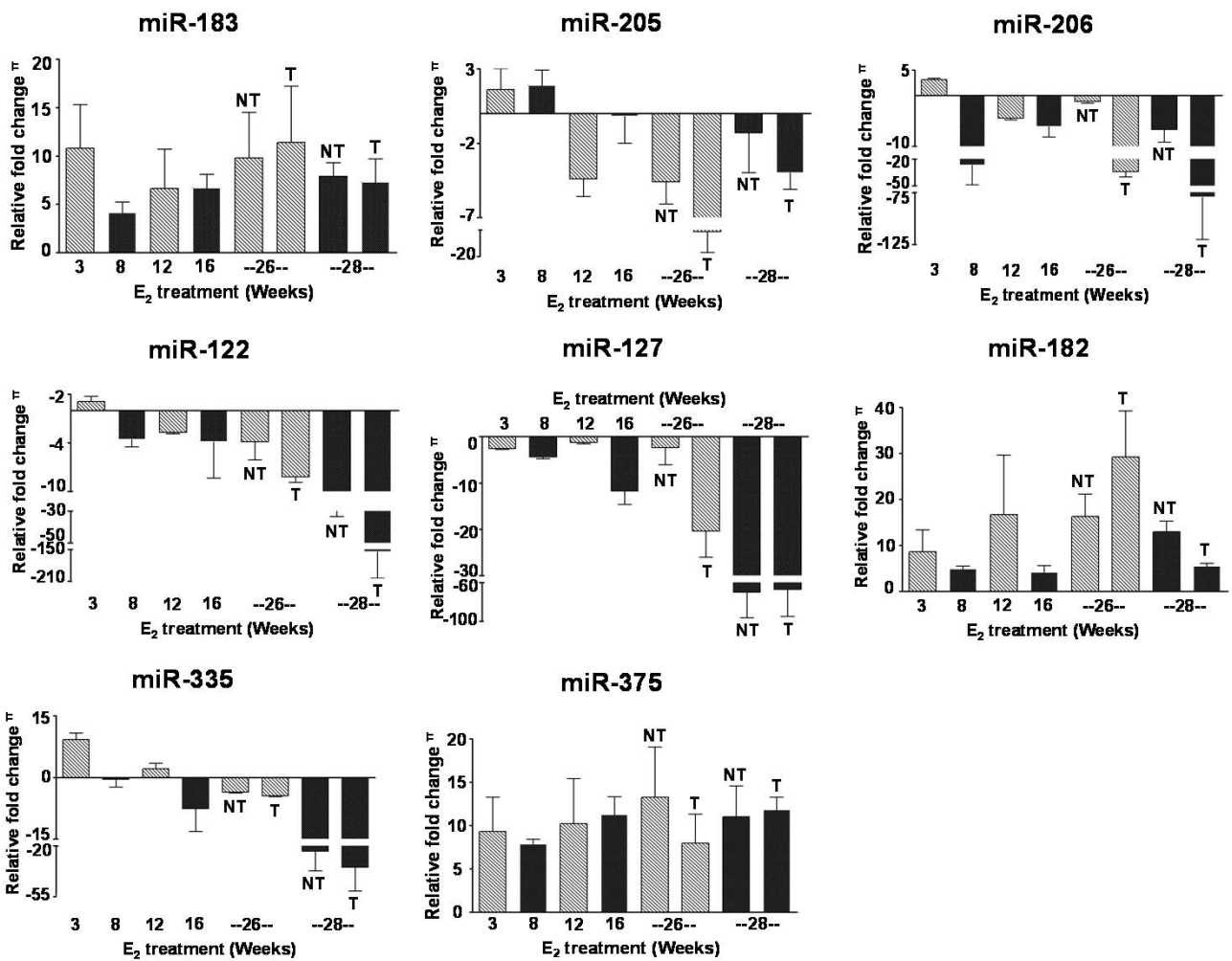
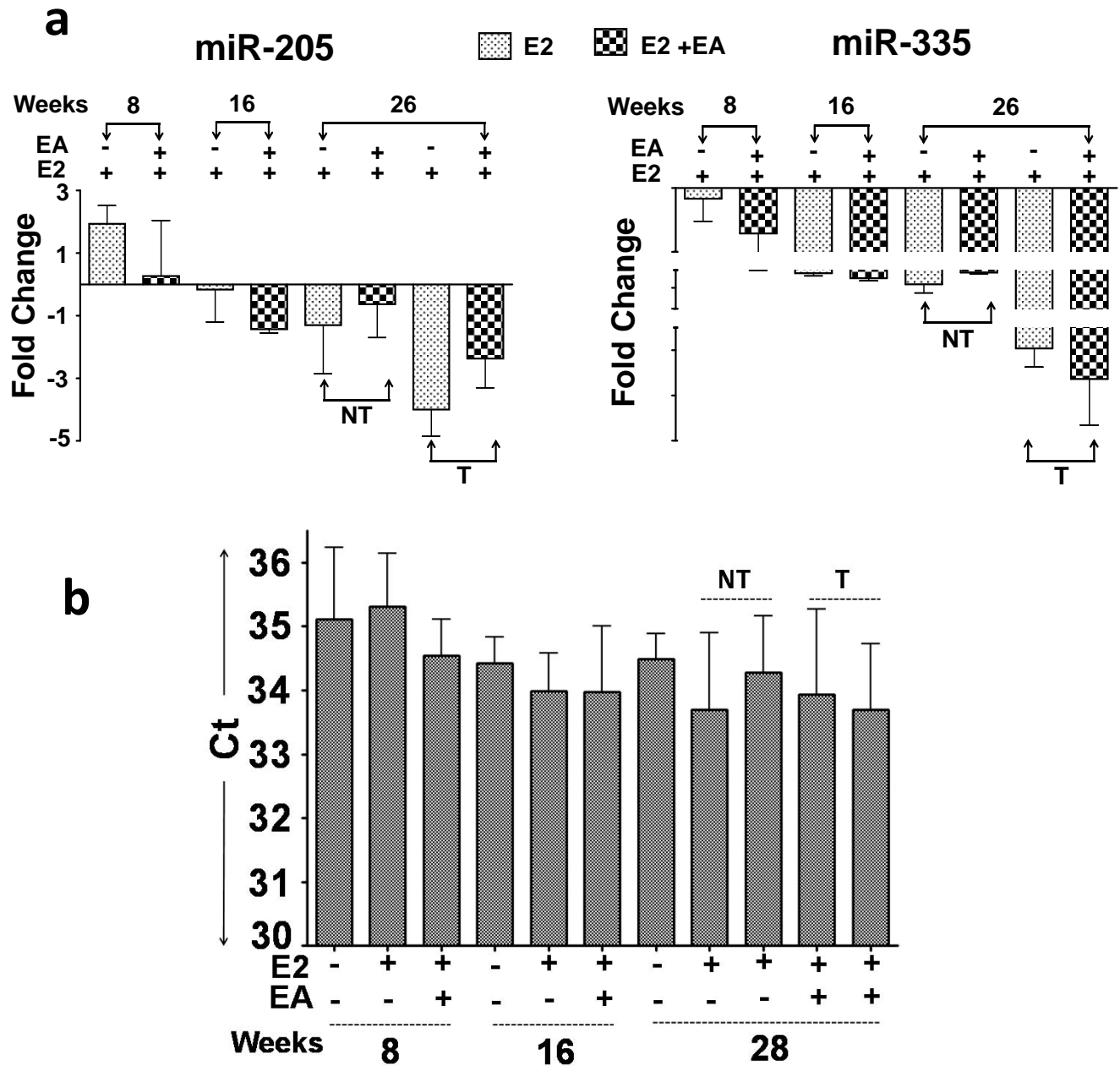


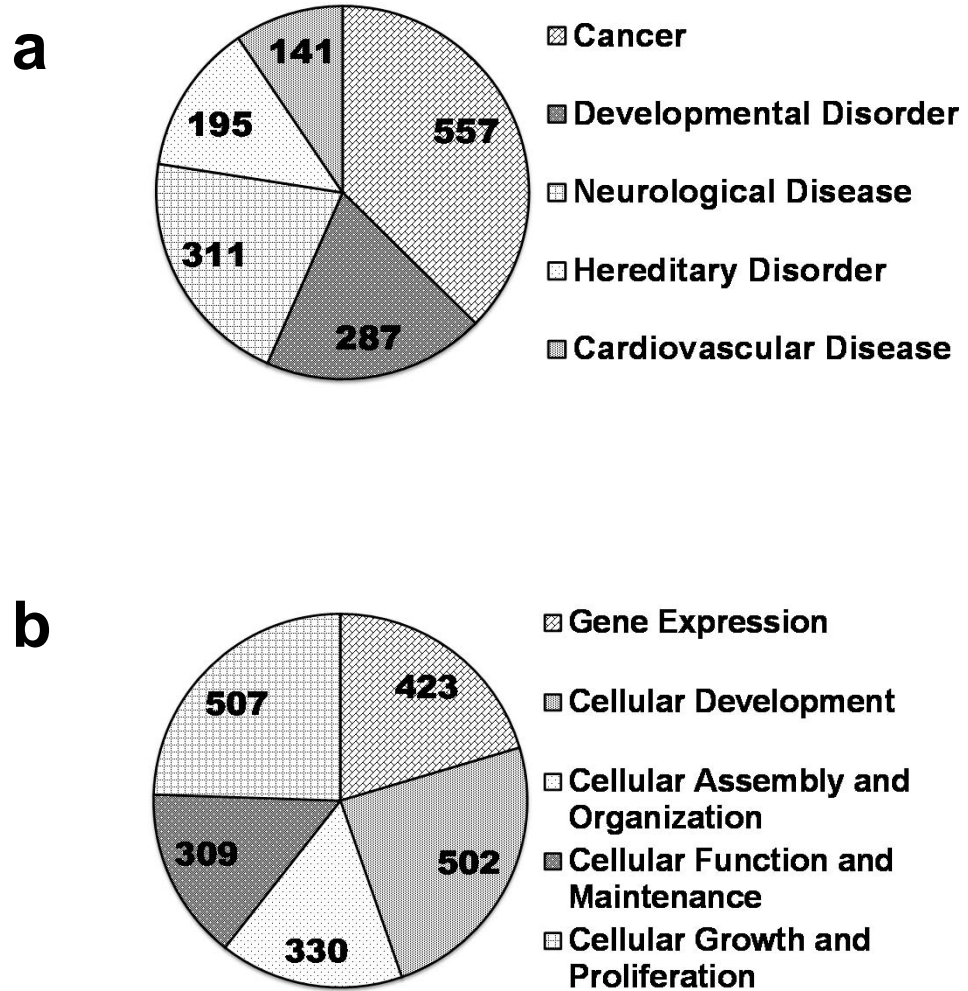
Figure S5: miRNA expression trends of between the Study 1 and Study 2.

# Supplementary Fig. S6



**Figure S6:** a) The effect of EA on miRNAs miR-205 and miR-335 did not attain statistical significance, b) The raw Ct values of housekeeping gene 5S rRNA of untreated, the E<sub>2</sub> alone and E<sub>2</sub>+EA at different time points showing no significant influence of E<sub>2</sub> alone or in combination with EA on its expression.

# Supplementary Fig. 7



**Figure S7:** The 5 top overrepresented - a) disorders; and b) molecular and cellular functions are shown. The number of targets involved in the functions is also represented in the pie-diagram.



**Supplementary Table 1:** List of miRNAs modulated significantly during estrogen mediated mammary carcinogenesis in female ACI rats

| S.No | Column ID                  | 3 Week  |             |
|------|----------------------------|---------|-------------|
|      |                            | p-value | Fold-Change |
| 1    | <b><i>rno-mir-1</i></b>    | 0.0158  | -15.23      |
| 2    | rno-mir-101a               | 0.0368  | 2.24        |
| 3    | rno-mir-106b               | 0.0059  | 1.98        |
| 4    | rno-mir-10a                | 0.0213  | 3.74        |
| 5    | rno-mir-10b                | 0.0471  | 4.37        |
| 6    | <b><i>rno-mir-122</i></b>  | 0.0244  | -2.70       |
| 7    | rno-mir-124                | 0.0110  | -13.88      |
| 8    | <b><i>rno-mir-127</i></b>  | 0.0128  | -3.15       |
| 9    | rno-mir-133b               | 0.0415  | -24.86      |
| 10   | <b><i>rno-mir-140</i></b>  | 0.0200  | 2.97        |
| 11   | rno-mir-15b                | 0.0378  | 2.92        |
| 12   | rno-miR-17                 | 0.0176  | 2.07        |
| 13   | rno-miR-17-3p              | 0.0218  | 2.18        |
| 14   | rno-miR-17-5p              | 0.0290  | 1.99        |
| 15   | <b><i>rno-mir-181c</i></b> | 0.0003  | 5.52        |
| 16   | <b><i>rno-mir-181d</i></b> | 0.0000  | 6.45        |
| 17   | <b><i>rno-mir-182</i></b>  | 0.0046  | 3.69        |
| 18   | <b><i>rno-mir-183</i></b>  | 0.0075  | 7.00        |
| 19   | <b><i>rno-mir-18a</i></b>  | 0.0004  | 4.81        |
| 20   | <b><i>rno-mir-196c</i></b> | 0.0000  | 44.54       |
| 21   | rno-mir-19a                | 0.0136  | 5.29        |
| 22   | rno-mir-19b                | 0.0005  | 2.89        |
| 23   | <b><i>rno-mir-200b</i></b> | 0.0213  | 3.54        |
| 24   | <b><i>rno-mir-200c</i></b> | 0.0136  | 2.96        |
| 25   | <b><i>rno-mir-205</i></b>  | 0.0140  | -1.98       |
| 26   | <b><i>rno-mir-206</i></b>  | 0.0238  | -9.56       |
| 27   | <b><i>rno-mir-20a</i></b>  | 0.0000  | 2.86        |
| 28   | rno-mir-21                 | 0.0405  | 5.36        |
| 29   | <b><i>rno-mir-25</i></b>   | 0.0010  | 2.96        |
| 30   | rno-mir-26b                | 0.0245  | -2.04       |
| 31   | rno-mir-26b                | 0.0437  | 2.87        |
| 32   | rno-mir-301a               | 0.0399  | 4.56        |
| 33   | <b><i>rno-mir-31</i></b>   | 0.0036  | 4.39        |
| 34   | rno-mir-327                | 0.0093  | -2.67       |
| 35   | rno-mir-329                | 0.0229  | -1.99       |
| 36   | rno-mir-331                | 0.0399  | 2.77        |

| S.No | Column ID                  | 12 Week |             |
|------|----------------------------|---------|-------------|
|      |                            | p-value | Fold-Change |
| 1    | <b><i>rno-mir-1</i></b>    | 2.3E-02 | -9.93       |
| 2    | rno-mir-106b               | 3.9E-02 | 1.63        |
| 3    | rno-mir-107                | 2.2E-02 | 1.55        |
| 4    | rno-mir-10a                | 2.3E-02 | -3.66       |
| 5    | <b><i>rno-mir-122</i></b>  | 6.6E-06 | -139.40     |
| 6    | rno-mir-124                | 2.1E-02 | -10.59      |
| 7    | rno-mir-125b               | 5.6E-03 | -3.05       |
| 8    | rno-mir-125b               | 3.6E-02 | -1.96       |
| 9    | <b><i>rno-mir-127</i></b>  | 3.6E-03 | -10.70      |
| 10   | rno-mir-129                | 3.7E-02 | 4.46        |
| 11   | rno-mir-132                | 4.6E-02 | -5.61       |
| 12   | rno-mir-134                | 6.4E-04 | -6.35       |
| 13   | <b><i>rno-mir-140</i></b>  | 9.7E-03 | -2.08       |
| 14   | <b><i>rno-mir-141</i></b>  | 4.0E-02 | 5.27        |
| 15   | rno-miR-17                 | 4.5E-02 | 1.87        |
| 16   | rno-miR-17-5p              | 3.4E-02 | 1.90        |
| 17   | rno-mir-181a               | 1.4E-02 | 2.46        |
| 18   | rno-mir-181b               | 1.6E-02 | 2.22        |
| 19   | <b><i>rno-mir-181c</i></b> | 2.0E-03 | 4.06        |
| 20   | <b><i>rno-mir-181d</i></b> | 1.0E-04 | 5.18        |
| 21   | <b><i>rno-mir-182</i></b>  | 3.2E-03 | 3.94        |
| 22   | <b><i>rno-mir-183</i></b>  | 2.8E-02 | 4.73        |
| 23   | <b><i>rno-mir-18a</i></b>  | 1.9E-02 | 2.57        |
| 24   | rno-mir-193                | 3.1E-03 | -4.39       |
| 25   | rno-mir-195                | 2.2E-02 | -1.93       |
| 26   | <b><i>rno-mir-196c</i></b> | 2.0E-03 | 13.99       |
| 27   | rno-mir-19b                | 3.5E-02 | 1.79        |
| 28   | <b><i>rno-mir-200a</i></b> | 1.0E-02 | 3.42        |
| 29   | <b><i>rno-mir-200c</i></b> | 4.0E-02 | 2.42        |
| 30   | <b><i>rno-mir-205</i></b>  | 1.3E-02 | -2.02       |
| 31   | <b><i>rno-mir-206</i></b>  | 2.7E-02 | -8.11       |
| 32   | <b><i>rno-mir-20a</i></b>  | 2.6E-02 | 1.55        |
| 33   | <b><i>rno-mir-214</i></b>  | 2.9E-03 | -3.54       |
| 34   | rno-mir-24                 | 1.5E-03 | -2.53       |
| 35   | rno-mir-25                 | 1.4E-02 | 2.13        |
| 36   | <b><i>rno-mir-25</i></b>   | 1.3E-02 | 2.16        |

|    |                         |        |       |
|----|-------------------------|--------|-------|
| 37 | rno-mir-342             | 0.0498 | 5.82  |
| 38 | rno-mir-347             | 0.0184 | -3.16 |
| 39 | <b>rno-mir-34a</b>      | 0.0008 | -3.02 |
| 40 | <b>rno-mir-34c</b>      | 0.0000 | 13.22 |
| 41 | <b>rno-mir-34c-star</b> | 0.0048 | 5.27  |
| 42 | rno-mir-384             | 0.0473 | -1.82 |
| 43 | rno-mir-410             | 0.0241 | -2.09 |
| 44 | <b>rno-mir-429</b>      | 0.0064 | 7.00  |
| 45 | rno-mir-434             | 0.0109 | -3.68 |
| 46 | rno-mir-455             | 0.0215 | 4.78  |
| 47 | rno-mir-485             | 0.0107 | -2.73 |
| 48 | rno-mir-487b            | 0.0202 | -3.45 |
| 49 | rno-mir-540             | 0.0263 | -2.03 |
| 50 | rno-mir-92a             | 0.0109 | 2.44  |
| 51 | <b>rno-mir-99a</b>      | 0.0049 | -1.96 |

|    |                         |         |       |
|----|-------------------------|---------|-------|
| 37 | rno-mir-29a             | 2.3E-04 | -1.92 |
| 38 | <b>rno-mir-29b</b>      | 2.3E-02 | -2.54 |
| 39 | <b>rno-mir-31</b>       | 2.4E-02 | 3.01  |
| 40 | <b>rno-mir-335</b>      | 2.5E-03 | -6.76 |
| 41 | <b>rno-mir-34a</b>      | 3.2E-04 | -3.35 |
| 42 | rno-mir-34b             | 9.9E-03 | 4.99  |
| 43 | <b>rno-mir-34c</b>      | 1.0E-03 | 6.82  |
| 44 | <b>rno-mir-34c-star</b> | 1.1E-05 | 20.46 |
| 45 | <b>rno-mir-375</b>      | 3.8E-03 | 8.99  |
| 46 | rno-mir-379             | 1.5E-02 | -7.96 |
| 47 | rno-mir-382             | 4.4E-03 | -6.63 |
| 48 | rno-mir-411             | 4.4E-02 | -2.71 |
| 49 | <b>rno-mir-429</b>      | 1.5E-02 | 3.77  |
| 50 | <b>rno-mir-489</b>      | 7.5E-03 | -3.61 |
| 51 | <b>rno-mir-497</b>      | 1.1E-02 | -2.64 |
| 52 | rno-mir-532             | 2.4E-02 | -2.50 |
| 53 | rno-mir-541             | 3.8E-02 | -3.41 |
| 54 | <b>rno-mir-672</b>      | 3.0E-02 | 4.11  |
| 55 | <b>rno-mir-708</b>      | 3.8E-02 | -3.62 |
| 56 | rno-mir-880             | 2.6E-02 | -1.64 |
| 57 | rno-mir-92a             | 1.2E-02 | 2.40  |
| 58 | <b>rno-mir-99a</b>      | 2.3E-04 | -2.59 |

| S.No | Column ID           | 26 Week (Non-tumor) |             |
|------|---------------------|---------------------|-------------|
|      |                     | p-value             | Fold-Change |
| 1    | <b>rno-mir-1</b>    | 0.0074              | -15.03      |
| 2    | rno-mir-103         | 0.0042              | 1.50        |
| 3    | rno-mir-106b        | 0.0177              | 1.56        |
| 4    | <b>rno-mir-122</b>  | 0.0228              | -4.85       |
| 5    | rno-mir-125b        | 0.0468              | -2.65       |
| 6    | rno-mir-125b-star   | 0.0091              | -2.24       |
| 7    | <b>rno-mir-127</b>  | 0.0007              | -9.18       |
| 8    | rno-mir-129         | 0.0202              | 4.37        |
| 9    | rno-mir-129-star    | 0.0024              | 6.03        |
| 10   | rno-mir-134         | 0.0231              | -2.40       |
| 11   | <b>rno-mir-140</b>  | 0.0021              | -2.01       |
| 12   | <b>rno-mir-141</b>  | 0.0015              | 8.56        |
| 13   | rno-mir-146b        | 0.0057              | 2.12        |
| 14   | rno-mir-154         | 0.0484              | -2.14       |
| 15   | rno-mir-17          | 0.0293              | 1.67        |
| 16   | rno-mir-17-5p       | 0.0292              | 1.70        |
| 17   | <b>rno-mir-181c</b> | 0.0159              | 2.24        |
| 18   | <b>rno-mir-181d</b> | 0.0000              | 5.60        |
| 19   | <b>rno-mir-182</b>  | 0.0000              | 5.96        |
| 20   | <b>rno-mir-183</b>  | 0.0001              | 11.79       |
| 21   | <b>rno-mir-18a</b>  | 0.0019              | 2.78        |
| 22   | rno-mir-193         | 0.0083              | -2.72       |
| 23   | rno-mir-195         | 0.0308              | -1.61       |
| 24   | <b>rno-mir-196c</b> | 0.0000              | 54.64       |
| 25   | rno-mir-19a         | 0.0254              | 3.17        |
| 26   | rno-mir-19b         | 0.0073              | 1.81        |
| 27   | <b>rno-mir-200a</b> | 0.0046              | 5.89        |
| 28   | <b>rno-mir-200b</b> | 0.0002              | 5.99        |
| 29   | <b>rno-mir-200c</b> | 0.0000              | 5.22        |
| 30   | <b>rno-mir-205</b>  | 0.0138              | -2.53       |
| 31   | <b>rno-mir-206</b>  | 0.0182              | -7.30       |
| 32   | <b>rno-mir-20a</b>  | 0.0001              | 1.92        |
| 33   | rno-mir-210         | 0.0157              | 2.70        |
| 34   | <b>rno-mir-214</b>  | 0.0022              | -2.75       |
| 35   | rno-mir-22          | 0.0125              | -2.00       |
| 36   | rno-mir-24          | 0.0155              | -1.68       |
| 37   | <b>rno-mir-25</b>   | 0.0091              | 1.88        |
| 38   | rno-mir-28          | 0.0443              | 1.67        |

| S.No | Column ID          | 26 Week (Tumor) |             |
|------|--------------------|-----------------|-------------|
|      |                    | p-value         | Fold-Change |
| 1    | <b>rno-mir-122</b> | 0.0000          | -105.28     |
| 2    | rno-mir-133a       | 0.0121          | -27.05      |
| 3    | <b>rno-mir-1</b>   | 0.0289          | -25.50      |
| 4    | rno-mir-139        | 0.0000          | -25.13      |
| 5    | <b>rno-mir-206</b> | 0.0298          | -24.83      |
| 6    | rno-mir-133b       | 0.0098          | -22.62      |
| 7    | <b>rno-mir-708</b> | 0.0000          | -21.89      |
| 8    | <b>rno-mir-335</b> | 0.0000          | -13.38      |
| 9    | rno-mir-150        | 0.0000          | -12.16      |
| 10   | <b>rno-mir-127</b> | 0.0001          | -12.02      |
| 11   | rno-mir-196a       | 0.0056          | -9.67       |
| 12   | rno-mir-199a       | 0.0000          | -9.37       |
| 13   | <b>rno-mir-214</b> | 0.0000          | -7.97       |
| 14   | rno-mir-138-2      | 0.0001          | -7.52       |
| 15   | rno-mir-379        | 0.0025          | -7.36       |
| 16   | rno-mir-124-1      | 0.0113          | -6.98       |
| 17   | rno-mir-10b        | 0.0012          | -6.93       |
| 18   | rno-mir-199a-star  | 0.0004          | -6.41       |
| 19   | rno-mir-196b       | 0.0008          | -5.79       |
| 20   | <b>rno-mir-497</b> | 0.0000          | -4.78       |
| 21   | <b>rno-mir-489</b> | 0.0001          | -4.67       |
| 22   | rno-mir-342-star   | 0.0237          | -4.62       |
| 23   | rno-mir-29c        | 0.0085          | -4.41       |
| 24   | rno-mir-100        | 0.0001          | -4.38       |
| 25   | rno-mir-10a        | 0.0014          | -4.25       |
| 26   | <b>rno-mir-29b</b> | 0.0001          | -3.85       |
| 27   | rno-mir-125b-3p    | 0.0001          | -3.69       |
| 28   | rno-mir-342        | 0.0144          | -3.44       |
| 29   | rno-mir-532        | 0.0003          | -3.32       |
| 30   | rno-mir-382        | 0.0136          | -3.26       |
| 31   | rno-mir-532-star   | 0.0064          | -3.09       |
| 32   | rno-mir-30e        | 0.0004          | -2.90       |
| 33   | rno-mir-541        | 0.0240          | -2.72       |
| 34   | rno-mir-30a        | 0.0152          | -2.71       |
| 35   | rno-mir-195        | 0.0001          | -2.70       |
| 36   | <b>rno-mir-193</b> | 0.0139          | -2.42       |
| 37   | <b>rno-mir-140</b> | 0.0126          | -2.40       |
| 38   | rno-mir-22         | 0.0018          | -2.38       |

|    |                         |        |       |
|----|-------------------------|--------|-------|
| 39 | <b>rno-mir-29b</b>      | 0.0036 | -2.62 |
| 40 | rno-mir-29c             | 0.0408 | -2.13 |
| 41 | <b>rno-mir-31</b>       | 0.0005 | 4.18  |
| 42 | rno-mir-329             | 0.0028 | -2.08 |
| 43 | <b>rno-mir-335</b>      | 0.0001 | -8.64 |
| 44 | rno-mir-338             | 0.0370 | -2.53 |
| 45 | rno-mir-344             | 0.0115 | 1.73  |
| 46 | rno-mir-34b             | 0.0117 | 3.36  |
| 47 | <b>rno-mir-34c</b>      | 0.0001 | 7.68  |
| 48 | <b>rno-mir-34c-star</b> | 0.0000 | 9.36  |
| 49 | <b>rno-mir-375</b>      | 0.0000 | 20.50 |
| 50 | rno-mir-379             | 0.0142 | -5.09 |
| 51 | rno-mir-383             | 0.0484 | -2.18 |
| 52 | <b>rno-mir-429</b>      | 0.0002 | 9.63  |
| 53 | <b>rno-mir-489</b>      | 0.0000 | -5.82 |
| 54 | <b>rno-mir-497</b>      | 0.0042 | -2.39 |
| 55 | rno-mir-532             | 0.0213 | -2.07 |
| 56 | rno-mir-541             | 0.0288 | -2.74 |
| 57 | <b>rno-mir-672</b>      | 0.0002 | 8.06  |
| 58 | <b>rno-mir-708</b>      | 0.0049 | -4.10 |
| 59 | rno-mir-93              | 0.0237 | 1.68  |
| 60 | rno-mir-96              | 0.0002 | 4.67  |
| 61 | <b>rno-mir-99a</b>      | 0.0002 | -2.09 |

|    |                     |        |       |
|----|---------------------|--------|-------|
| 39 | rno-mir-125b-5p     | 0.0012 | -2.30 |
| 40 | rno-mir-154         | 0.0269 | -2.28 |
| 41 | rno-mir-30e         | 0.0338 | -2.21 |
| 42 | rno-mir-142         | 0.0152 | -2.16 |
| 43 | rno-mir-339         | 0.0420 | -2.14 |
| 44 | <b>rno-mir-99a</b>  | 0.0001 | -2.12 |
| 45 | rno-mir-29a         | 0.0000 | -2.06 |
| 46 | rno-mir-370         | 0.0156 | -2.05 |
| 47 | rno-mir-134         | 0.0492 | -2.04 |
| 48 | rno-mir-126         | 0.0021 | -2.03 |
| 49 | rno-mir-378         | 0.0355 | -2.02 |
| 50 | rno-mir-27b         | 0.0004 | -1.92 |
| 51 | rno-mir-152         | 0.0063 | -1.90 |
| 52 | rno-mir-27a         | 0.0003 | -1.89 |
| 53 | rno-mir-24          | 0.0043 | -1.83 |
| 54 | rno-mir-222         | 0.0329 | -1.78 |
| 55 | rno-mir-378-star    | 0.0223 | -1.73 |
| 56 | rno-mir-143         | 0.0120 | -1.73 |
| 57 | rno-mir-145         | 0.0093 | -1.72 |
| 58 | rno-mir-329         | 0.0222 | -1.67 |
| 59 | rno-mir-142-star    | 0.0238 | -1.59 |
| 60 | rno-mir-146a        | 0.0320 | -1.57 |
| 61 | <b>rno-mir-34a</b>  | 0.0386 | -1.54 |
| 62 | rno-mir-130a        | 0.0500 | -1.53 |
| 63 | rno-mir-30c         | 0.0054 | -1.52 |
| 64 | rno-mir-107         | 0.0057 | 1.50  |
| 65 | <b>rno-mir-205</b>  | 0.0199 | -1.55 |
| 66 | rno-mir-19b         | 0.0180 | 1.63  |
| 67 | <b>rno-mir-181c</b> | 0.0091 | 1.68  |
| 68 | rno-mir-17-1        | 0.0032 | 2.01  |
| 69 | rno-mir-28          | 0.0003 | 2.02  |
| 70 | rno-mir-483         | 0.0043 | 2.02  |
| 71 | rno-mir-125a        | 0.0114 | 2.05  |
| 72 | rno-mir-17-1 -star  | 0.0026 | 2.10  |
| 73 | rno-mir-96          | 0.0342 | 2.11  |
| 74 | rno-mir-297         | 0.0203 | 2.16  |
| 75 | <b>rno-mir-20a</b>  | 0.0000 | 2.18  |
| 76 | rno-mir-28-star     | 0.0024 | 2.22  |
| 77 | rno-mir-673         | 0.0333 | 2.25  |
| 78 | <b>rno-mir-25</b>   | 0.0009 | 2.26  |
| 79 | rno-mir-330         | 0.0483 | 2.28  |

|     |                         |        |       |
|-----|-------------------------|--------|-------|
| 80  | rno-mir-99b             | 0.0389 | 2.39  |
| 81  | rno-mir-21              | 0.0469 | 2.45  |
| 82  | rno-mir-106b            | 0.0158 | 2.46  |
| 83  | rno-mir-760             | 0.0358 | 2.49  |
| 84  | rno-mir-106b-star       | 0.0000 | 2.58  |
| 85  | rno-mir-93              | 0.0001 | 2.59  |
| 86  | rno-mir-203             | 0.0492 | 2.69  |
| 87  | rno-mir-34b             | 0.0273 | 2.71  |
| 88  | rno-mir-598             | 0.0403 | 2.89  |
| 89  | <b>rno-mir-18a</b>      | 0.0003 | 3.29  |
| 90  | rno-mir-130b            | 0.0269 | 3.61  |
| 91  | rno-mir-351             | 0.0039 | 3.84  |
| 92  | <b>rno-mir-31</b>       | 0.0003 | 4.16  |
| 93  | rno-mir-503             | 0.0045 | 4.50  |
| 94  | rno-mir-204             | 0.0145 | 4.52  |
| 95  | rno-mir-210             | 0.0004 | 4.57  |
| 96  | rno-mir-146b            | 0.0000 | 4.89  |
| 97  | rno-mir-322             | 0.0141 | 5.04  |
| 98  | rno-mir-542             | 0.0022 | 5.56  |
| 99  | <b>rno-mir-200c</b>     | 0.0000 | 5.74  |
| 100 | rno-mir-204-star        | 0.0016 | 6.00  |
| 101 | <b>rno-mir-200a</b>     | 0.0016 | 6.92  |
| 102 | <b>rno-mir-200b</b>     | 0.0000 | 7.38  |
| 103 | <b>rno-mir-196c</b>     | 0.0011 | 8.08  |
| 104 | <b>rno-mir-672</b>      | 0.0001 | 8.11  |
| 105 | <b>rno-mir-181d</b>     | 0.0000 | 8.74  |
| 106 | <b>rno-mir-141</b>      | 0.0008 | 9.12  |
| 107 | <b>rno-mir-182</b>      | 0.0000 | 9.14  |
| 108 | <b>rno-mir-34c</b>      | 0.0000 | 9.30  |
| 109 | <b>rno-mir-34c-star</b> | 0.0000 | 9.44  |
| 110 | <b>rno-mir-429</b>      | 0.0001 | 10.47 |
| 111 | <b>rno-mir-183</b>      | 0.0000 | 13.15 |
| 112 | <b>rno-mir-375</b>      | 0.0000 | 15.43 |
| 113 | rno-mir-129-2           | 0.0000 | 30.98 |
| 114 | rno-mir-129-2-star      | 0.0000 | 32.87 |

**Supplementary Table 2: Top Biofunctions and Canonical Pathways of aberrant miRNAs**

|   | 3 Wk                |                    | 12 wk               |                    | 26 Wk N             |                    | 26 Wk T             |                    |
|---|---------------------|--------------------|---------------------|--------------------|---------------------|--------------------|---------------------|--------------------|
| <b>TOP BIO FUNCTIONS</b>                | <b>p-value</b>      | <b># Molecules</b> | <b>p-value</b>      | <b># Molecules</b> | <b>p-value</b>      | <b># Molecules</b> | <b>p-value</b>      | <b># Molecules</b> |
| <b>Diseases and Disorders</b>           |                     |                    |                     |                    |                     |                    |                     |                    |
| Cancer                                  | 9.37E-31 - 4.98E-07 | 1653               | 2.76E-37 - 4.39E-07 | 1722               | 6.45E-33 - 4.41E-07 | 1597               | 7.54E-34 - 1.58E-07 | 2252               |
| Developmental Disease                   | 2.40E-32 - 4.21E-07 | 818                | 5.98E-33 - 9.93E-08 | 771                | 7.86E-28 - 5.29E-07 | 714                | 2.52E-39 - 7.99E-08 | 933                |
| Neurological Disease                    | 1.01E-27 - 6.95E-08 | 1008               | 3.79E-25 - 3.42E-07 | 968                | 5.85E-20 - 2.01E-07 | 887                | 4.39E-32 - 1.02E-07 | 1213               |
| Hereditary Disorder                     | 8.13E-19 - 6.95E-08 | 528                | 1.99E-19 - 2.14E-10 | 506                | 3.57E-14 - 1.07E-08 | 452                | 4.55E-22 - 1.43E-11 | 606                |
| Skeletal and Muscular Disorders         | 8.13E-19 - 1.60E-07 | 524                | 1.99E-19 - 3.06E-07 | 578                | 3.57E-14 - 2.63E-08 | 529                | 4.55E-22 - 2.24E-08 | 649                |
|   |                     |                    |                     |                    |                     |                    |                     |                    |
| <b>Molecular and Cellular Functions</b> |                     |                    |                     |                    |                     |                    |                     |                    |
| Gene Expression                         | 2.98E-60 - 1.45E-07 | 1105               | 3.84E-75 - 5.12E-10 | 1192               | 6.48E-73 - 7.91E-12 | 1115               | 9.88E-75 - 2.09E-08 | 1347               |
| Cellular Assembly and Organization      | 3.20E-50 - 3.91E-07 | 898                | 5.32E-56 - 3.32E-07 | 953                | 3.17E-54 - 3.03E-07 | 895                | 4.29E-57 - 7.12E-08 | 1079               |
| Cellular Function and Maintenance       | 3.20E-50 - 1.79E-07 | 1195               | 5.32E-56 - 3.32E-07 | 1296               | 3.17E-54 - 3.49E-07 | 1177               | 4.29E-57 - 1.17E-07 | 1438               |
| Cellular Development                    | 2.06E-45 - 5.84E-07 | 1428               | 4.92E-44 - 3.20E-07 | 1508               | 3.10E-46 - 4.80E-07 | 1425               | 4.35E-51 - 1.33E-07 | 1783               |
| Cell Morphology                         | 1.30E-42 - 5.69E-07 | 1150               | 8.97E-45 - 3.02E-07 | 1205               | 1.99E-41 - 2.00E-07 | 1117               | 8.63E-49 - 1.39E-07 | 1734               |
|   |                     |                    |                     |                    |                     |                    |                     |                    |
| <b>TOP CANONICAL PATHWAYS</b>           | <b>p-value</b>      | <b>Ratio</b>       | <b>p-value</b>      | <b>Ratio</b>       | <b>p-value</b>      | <b>Ratio</b>       | <b>p-value</b>      | <b>Ratio</b>       |
|   |                     |                    |                     |                    |                     |                    |                     |                    |
| Molecular Mechanism of Cancer           | 3.22E-24            | 185/366 (0.505)    | 2.41E-24            | 186/378 (0.492)    | 8.19E-20            | 167/378 (0.442)    | 4.27E-25            | 255/430 (0.563)    |
| Axonal Guidance Signaling               | 2.06E-35            | 227/422 (0.538)    | 1.31E-30            | 219/430 (0.509)    | 1.84E-27            | 202/430 (0.470)    | 4.49E-34            | 213/378 (0.593)    |
| HGF Signaling                           | 3.69E-18            | 70/102 (0.686)     | 9.82E-16            | 67/105 (0.638)     | 1.44E-15            | 64/105 (0.610)     | 1.70E-18            | 106/162 (0.654)    |
| Ephrin Receptor Signaling               | 1.09E-16            | 101/195 (0.518)    | 3.39E-18            | 104/199 (0.523)    | 2.84E-15            | 94/199 (0.472)     | 3.48E-18            | 117/195 (0.600)    |