Article

Genetic regulation of human isomiR biogenesis

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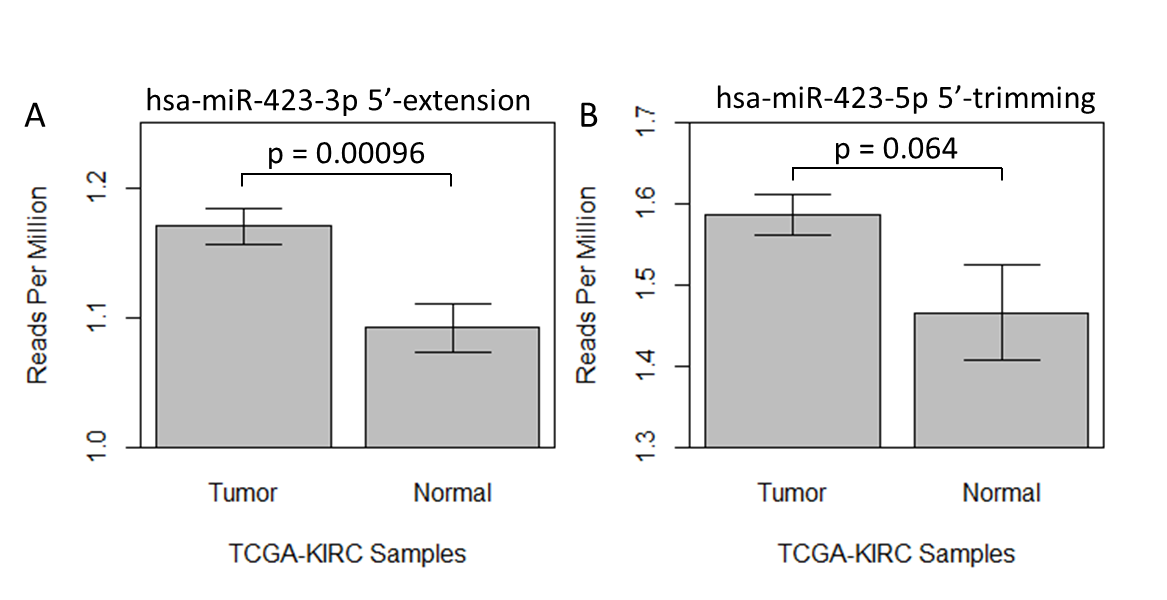
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**Supplemental figure 1. Scatter plot of the first two principal components for 1000 Genomes project subjects.** Subjects included in this study are highlighted in colors.  
CEU: Utah residents with Northern and Western European ancestry, European Ancestry  
FIN: Finnish in Finland, European Ancestry  
GRB: British in England and Scotland, European Ancestry  
TSI: Toscani in Italy, European Ancestry  
YRI: Yoruba in Ibadan, Nigeria, African Ancestry

A graph with numbers and a number of dots

Description automatically generated

**Supplemental figure 2. isomiR expression in TCGA kidney renal clear cell carcinoma.** Barplot for average expression and standard error for A) hsa-miR-423-3p 5’-extension isomiRs and B) hsa-miR-423-5p 5’-trimming isomiRs in TCGA kidney renal clear cell carcinoma (TCGA-KIRC) and normal samples.

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**Supplementary table 1.** Correlation results between SNPs and isomiRs composition with FDR < 0.05 in all subjects, and FDR<0.05 in either European or African subjects.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP** | **isomiR** | | | | **All(n=435)** | | | **European(n=348)** | | | **African(n=87)** | | |
| **rsID** | **miRNA** | **subtype** | **#isomiR** | **#base change** | **Tau** | **p-value** | **FDR** | **Tau** | **p-value** | **FDR** | **Tau** | **p-value** | **FDR** |
| rs641071 | hsa-miR-4482-3p | 5-sub | 1 | 0 | -0.64 | 5.4E-60 | 4.5E-57 | -0.59 | 7.0E-39 | 3.4E-36 | -0.30 | 7.8E-04 | 0.012 |
| rs641071 | hsa-miR-4482-3p | 5-trim | 1 | -1 | -0.63 | 5.7E-59 | 2.4E-56 | -0.59 | 1.0E-38 | 3.4E-36 | -0.24 | 0.0054 | 0.066 |
| rs641071 | hsa-miR-4482-3p | 5-trim | 1 | -2 | -0.63 | 8.8E-59 | 2.5E-56 | -0.59 | 1.8E-38 | 4.0E-36 | -0.21 | 0.016 | 0.15 |
| rs641071 | hsa-miR-4482-3p | 5-ext | 1 | 1 | -0.63 | 4.7E-58 | 9.8E-56 | -0.57 | 1.6E-36 | 2.6E-34 | -0.29 | 0.0012 | 0.017 |
| rs2273626 | hsa-miR-4707-3p | 5-ext | 1 | 1 | 0.50 | 1.0E-34 | 1.7E-32 | 0.51 | 2.4E-27 | 2.7E-25 | 0.20 | 0.035 | 0.26 |
| rs2155248 | hsa-miR-1304-3p | 5-trim | 3 | -5 | -0.47 | 3.1E-33 | 4.3E-31 | -0.13 | 0.0025 | 0.024 | -0.59 | 4.2E-12 | 2.9E-09 |
| rs2155248 | hsa-miR-1304-3p | 5-trim | 2 | -4 | -0.46 | 6.7E-33 | 7.4E-31 | -0.13 | 0.0025 | 0.024 | -0.58 | 8.7E-12 | 3.0E-09 |
| rs34115976 | hsa-miR-577 | 5-ext | 15 | 1 | -0.47 | 7.1E-33 | 7.4E-31 | -0.49 | 9.5E-29 | 1.2E-26 | -0.17 | 0.057 | 0.36 |
| rs2168518 | hsa-miR-4513 | 5-add | 3 | 4 | 0.44 | 2.7E-30 | 2.5E-28 | 0.37 | 6.9E-17 | 3.3E-15 | NA | NA | NA |
| rs2155248 | hsa-miR-1304-3p | 5-ext | 24 | 2 | 0.44 | 5.4E-30 | 4.5E-28 | 0.15 | 6.2E-04 | 0.0077 | 0.57 | 1.5E-11 | 3.6E-09 |
| rs2155248 | hsa-miR-1304-3p | 5-trim | 6 | -3 | -0.43 | 4.1E-28 | 3.1E-26 | -0.11 | 0.014 | 0.098 | -0.49 | 9.7E-09 | 1.4E-06 |
| rs487571 | hsa-miR-5680 | 5-ext | 9 | 2 | 0.40 | 3.1E-26 | 2.1E-24 | 0.39 | 3.6E-20 | 2.6E-18 | 0.41 | 1.2E-06 | 8.5E-05 |
| rs10061133 | hsa-miR-449b-5p | 5-sub | 2 | 0 | -0.46 | 1.5E-23 | 1.0E-21 | -0.48 | 3.1E-20 | 2.6E-18 | -0.30 | 0.0051 | 0.062 |
| rs6505162 | hsa-miR-423-3p | 5-ext | 28 | 2 | -0.37 | 4.9E-23 | 3.0E-21 | -0.33 | 2.2E-15 | 9.6E-14 | -0.20 | 0.025 | 0.20 |
| rs28664200 | hsa-miR-1255a | 5-trim | 1 | -1 | 0.38 | 1.7E-21 | 9.5E-20 | 0.42 | 7.7E-21 | 7.2E-19 | 0.25 | 0.0050 | 0.062 |
| rs6505162 | hsa-miR-423-5p | 5-trim | 20 | -2 | -0.33 | 4.6E-19 | 2.4E-17 | -0.30 | 6.5E-13 | 2.4E-11 | -0.37 | 2.2E-05 | 9.0E-04 |
| rs2155248 | hsa-miR-1304-3p | 5-ext | 22 | 1 | 0.34 | 6.3E-19 | 3.0E-17 | 0.14 | 0.0018 | 0.019 | 0.50 | 3.0E-09 | 5.2E-07 |
| rs7208391 | hsa-miR-6868-3p | 5-ext | 2 | 1 | 0.38 | 6.4E-19 | 3.0E-17 | 0.34 | 2.6E-13 | 1.0E-11 | 0.45 | 6.1E-06 | 3.3E-04 |
| rs7911488 | hsa-miR-1307-3p | 5-trim | 131 | -1 | -0.33 | 3.2E-18 | 1.4E-16 | -0.32 | 3.3E-14 | 1.4E-12 | -0.10 | 0.25 | 0.78 |
| rs2155248 | hsa-miR-1304-3p | 5-trim | 54 | -1 | -0.33 | 2.7E-17 | 1.1E-15 | -0.11 | 0.0095 | 0.077 | -0.32 | 1.9E-04 | 0.0039 |
| rs8054514 | hsa-miR-3176 | 5-ext | 2 | 1 | 0.31 | 8.1E-16 | 3.2E-14 | 0.26 | 4.0E-09 | 1.3E-07 | 0.46 | 6.6E-08 | 6.6E-06 |
| rs75538180 | hsa-miR-1303 | 5-ext | 26 | 1 | 0.28 | 5.4E-14 | 2.0E-12 | 0.25 | 2.2E-09 | 7.2E-08 | 0.32 | 2.0E-04 | 0.0039 |
| rs8054514 | hsa-miR-3176 | 5-add | 1 | 3 | 0.29 | 5.4E-14 | 2.0E-12 | 0.25 | 1.3E-08 | 3.4E-07 | 0.47 | 3.2E-08 | 3.7E-06 |
| rs75538180 | hsa-miR-1303 | 5-ext | 4 | 2 | -0.28 | 6.6E-14 | 2.3E-12 | -0.22 | 1.5E-07 | 3.2E-06 | -0.22 | 0.011 | 0.11 |
| rs77639117 | hsa-miR-576-5p | 5-trim | 4 | -1 | 0.29 | 9.0E-14 | 3.0E-12 | 0.26 | 4.4E-09 | 1.3E-07 | 0.41 | 3.1E-06 | 1.8E-04 |
| rs8054514 | hsa-miR-3176 | 5-trim | 3 | -1 | 0.28 | 4.8E-13 | 1.6E-11 | 0.25 | 1.8E-08 | 4.5E-07 | 0.44 | 2.4E-07 | 2.1E-05 |
| rs174561 | hsa-miR-1908-5p | 5-trim | 1 | -1 | -0.26 | 2.8E-11 | 8.8E-10 | -0.29 | 3.2E-11 | 1.1E-09 | -0.15 | 0.094 | 0.49 |
| rs7227168 | hsa-miR-4741 | 5-ext | 1 | 3 | 0.26 | 1.1E-10 | 3.2E-09 | 0.26 | 1.8E-08 | 4.5E-07 | 0.32 | 4.3E-04 | 0.0071 |
| rs487571 | hsa-miR-5680 | 5-trim | 2 | -8 | 0.24 | 5.9E-10 | 1.7E-08 | 0.22 | 1.4E-07 | 2.9E-06 | 0.23 | 0.0069 | 0.075 |
| rs487571 | hsa-miR-5680 | 5-trim | 2 | -3 | 0.22 | 8.2E-09 | 2.3E-07 | 0.20 | 3.9E-06 | 7.0E-05 | 0.30 | 3.9E-04 | 0.0068 |
| rs487571 | hsa-miR-5680 | 5-ext | 1 | 3 | 0.22 | 1.0E-08 | 2.8E-07 | 0.21 | 1.0E-06 | 1.9E-05 | 0.22 | 0.011 | 0.11 |
| rs8054514 | hsa-miR-3176 | 5-sub | 6 | 0 | 0.22 | 1.1E-08 | 2.9E-07 | 0.17 | 6.7E-05 | 0.0011 | 0.41 | 1.7E-06 | 1.1E-04 |
| rs2682818 | hsa-miR-618 | 5-trim | 1 | -6 | 0.22 | 1.3E-08 | 3.3E-07 | 0.25 | 1.2E-08 | 3.4E-07 | 0.34 | 7.9E-05 | 0.0022 |
| rs74085143 | hsa-miR-4781-3p | 5-trim | 5 | -2 | 0.23 | 1.3E-08 | 3.3E-07 | 0.14 | 0.0018 | 0.019 | 0.39 | 1.2E-05 | 5.7E-04 |
| rs487571 | hsa-miR-5680 | 5-ext | 1 | 7 | 0.21 | 1.7E-08 | 4.0E-07 | 0.21 | 1.3E-06 | 2.4E-05 | 0.20 | 0.019 | 0.17 |
| rs487571 | hsa-miR-5680 | 5-ext | 2 | 5 | 0.20 | 7.5E-08 | 1.7E-06 | 0.19 | 7.9E-06 | 1.3E-04 | 0.22 | 0.0089 | 0.096 |
| rs2682818 | hsa-miR-618 | 5-trim | 1 | -7 | 0.21 | 8.0E-08 | 1.8E-06 | 0.24 | 3.7E-08 | 9.0E-07 | 0.32 | 2.0E-04 | 0.0039 |
| rs487571 | hsa-miR-5680 | 5-trim | 1 | -4 | 0.20 | 8.0E-08 | 1.8E-06 | 0.19 | 6.6E-06 | 1.1E-04 | 0.21 | 0.012 | 0.12 |
| rs2682818 | hsa-miR-618 | 5-trim | 2 | -1 | 0.21 | 8.7E-08 | 1.9E-06 | 0.24 | 4.0E-08 | 9.2E-07 | 0.35 | 6.8E-05 | 0.0022 |
| rs2682818 | hsa-miR-618 | 5-trim | 2 | -3 | 0.21 | 9.7E-08 | 2.0E-06 | 0.24 | 3.9E-08 | 9.1E-07 | 0.32 | 2.9E-04 | 0.0054 |
| rs4822739 | hsa-miR-548j-5p | 5-sub | 2 | 0 | -0.22 | 1.0E-07 | 2.1E-06 | -0.11 | 0.018 | 0.12 | -0.40 | 8.6E-06 | 4.3E-04 |
| rs487571 | hsa-miR-5680 | 5-trim | 6 | -1 | 0.20 | 2.0E-07 | 3.9E-06 | 0.17 | 8.4E-05 | 0.0013 | 0.32 | 1.5E-04 | 0.0036 |
| rs7911488 | hsa-miR-1307-3p | 5-trim | 2 | -6 | 0.20 | 2.1E-07 | 4.1E-06 | 0.15 | 5.0E-04 | 0.0064 | 0.12 | 0.16 | 0.63 |
| rs9589207 | hsa-miR-92a-1-5p | 5-trim | 5 | -2 | -0.20 | 2.7E-07 | 5.1E-06 | NA | NA | NA | -0.43 | 1.1E-06 | 8.5E-05 |
| rs5997893 | hsa-miR-3928-3p | 5-trim | 33 | -2 | -0.20 | 2.7E-07 | 5.1E-06 | -0.13 | 0.0025 | 0.024 | -0.11 | 0.21 | 0.70 |
| rs2682818 | hsa-miR-618 | 5-trim | 2 | -5 | 0.20 | 3.5E-07 | 6.3E-06 | 0.23 | 2.5E-07 | 5.0E-06 | 0.36 | 4.3E-05 | 0.0015 |
| rs2682818 | hsa-miR-618 | 5-trim | 2 | -4 | 0.19 | 8.1E-07 | 1.4E-05 | 0.23 | 1.4E-07 | 2.9E-06 | 0.30 | 5.2E-04 | 0.0085 |
| rs151318590 | hsa-miR-500b-3p | 5-ext | 2 | 2 | -0.22 | 1.1E-06 | 2.0E-05 | NA | NA | NA | -0.42 | 1.7E-05 | 7.3E-04 |
| rs4822739 | hsa-miR-548j-5p | 5-add | 2 | 1 | -0.20 | 1.4E-06 | 2.3E-05 | -0.09 | 0.048 | 0.26 | -0.37 | 4.4E-05 | 0.0015 |
| rs9589207 | hsa-miR-92a-1-5p | 5-trim | 3 | -3 | -0.19 | 1.7E-06 | 2.8E-05 | NA | NA | NA | -0.33 | 1.6E-04 | 0.0036 |
| rs151318590 | hsa-miR-500b-3p | 5-trim | 1 | -4 | -0.21 | 1.8E-06 | 2.9E-05 | NA | NA | NA | -0.40 | 3.4E-05 | 0.0013 |
| rs2682818 | hsa-miR-618 | 5-trim | 3 | -2 | 0.19 | 1.9E-06 | 3.0E-05 | 0.22 | 4.9E-07 | 9.5E-06 | 0.30 | 5.6E-04 | 0.0089 |
| rs7911488 | hsa-miR-1307-3p | 5-trim | 2 | -7 | 0.18 | 2.4E-06 | 3.6E-05 | 0.14 | 8.2E-04 | 0.0096 | 0.05 | 0.58 | 0.88 |
| rs74085143 | hsa-miR-4781-3p | 5-trim | 3 | -1 | 0.19 | 2.7E-06 | 4.0E-05 | 0.11 | 0.020 | 0.13 | 0.35 | 7.8E-05 | 0.0022 |
| rs9589207 | hsa-miR-92a-1-5p | 5-trim | 3 | -1 | -0.18 | 3.0E-06 | 4.4E-05 | NA | NA | NA | -0.34 | 1.0E-04 | 0.0026 |
| rs74085143 | hsa-miR-4781-3p | 5-trim | 1 | -4 | 0.19 | 4.3E-06 | 6.2E-05 | 0.12 | 0.0095 | 0.077 | 0.35 | 9.3E-05 | 0.0025 |
| rs1439619 | hsa-miR-3175 | 5-add | 1 | 4 | -0.20 | 4.5E-06 | 6.3E-05 | -0.22 | 7.7E-06 | 1.3E-04 | -0.13 | 0.18 | 0.65 |
| rs4822739 | hsa-miR-548j-5p | 5-ext | 1 | 8 | -0.19 | 5.1E-06 | 7.2E-05 | -0.08 | 0.082 | 0.34 | -0.36 | 7.8E-05 | 0.0022 |
| rs35613341 | hsa-miR-5189-5p | 5-trim | 1 | -1 | 0.20 | 6.5E-06 | 9.0E-05 | 0.21 | 4.0E-05 | 6.4E-04 | 0.20 | 0.040 | 0.27 |
| rs4822739 | hsa-miR-548j-5p | 5-add | 1 | 2 | -0.18 | 1.2E-05 | 1.5E-04 | -0.08 | 0.080 | 0.34 | -0.35 | 1.3E-04 | 0.0032 |
| rs10422347 | hsa-miR-4745-5p | 5-add | 1 | 2 | 0.18 | 1.3E-05 | 1.6E-04 | 0.18 | 9.2E-05 | 0.0014 | 0.13 | 0.14 | 0.59 |
| rs4534339 | hsa-miR-1843 | 5-ext | 29 | 1 | -0.17 | 1.3E-05 | 1.6E-04 | -0.09 | 0.034 | 0.20 | -0.29 | 7.7E-04 | 0.012 |
| rs9589207 | hsa-miR-92a-1-5p | 5-ext | 1 | 1 | -0.17 | 1.4E-05 | 1.8E-04 | NA | NA | NA | -0.28 | 0.0013 | 0.018 |
| rs4822739 | hsa-miR-548j-3p | 5-trim | 1 | -2 | -0.20 | 1.6E-05 | 2.0E-04 | -0.05 | 0.39 | 0.67 | -0.38 | 1.9E-04 | 0.0039 |
| rs7911488 | hsa-miR-1307-3p | 5-add | 4 | 1 | 0.16 | 1.6E-05 | 2.0E-04 | 0.15 | 4.0E-04 | 0.0054 | 0.02 | 0.86 | 0.98 |
| rs9589207 | hsa-miR-92a-1-5p | 5-trim | 1 | -4 | -0.17 | 1.8E-05 | 2.2E-04 | NA | NA | NA | -0.28 | 0.0018 | 0.024 |
| rs151318590 | hsa-miR-500b-3p | 5-trim | 1 | -3 | -0.19 | 2.0E-05 | 2.3E-04 | NA | NA | NA | -0.34 | 4.0E-04 | 0.0068 |
| rs2620381 | hsa-miR-627-5p | 5-trim | 6 | -1 | -0.17 | 2.1E-05 | 2.5E-04 | -0.06 | 0.17 | 0.46 | -0.32 | 3.9E-04 | 0.0068 |
| rs151318590 | hsa-miR-500b-3p | 5-ext | 1 | 1 | -0.19 | 2.4E-05 | 2.8E-04 | NA | NA | NA | -0.35 | 3.2E-04 | 0.0059 |
| rs9589207 | hsa-miR-92a-1-5p | 5-sub | 21 | 0 | -0.16 | 3.1E-05 | 3.5E-04 | NA | NA | NA | -0.33 | 1.9E-04 | 0.0039 |
| rs56292801 | hsa-miR-5189-5p | 5-trim | 1 | -1 | 0.19 | 3.9E-05 | 4.4E-04 | 0.18 | 3.0E-04 | 0.0043 | 0.19 | 0.060 | 0.37 |
| rs9589207 | hsa-miR-92a-1-5p | 5-add | 1 | 1 | -0.16 | 4.9E-05 | 5.4E-04 | NA | NA | NA | -0.28 | 0.0014 | 0.019 |
| rs2427556 | hsa-miR-941 | 5-add | 2 | 1 | 0.15 | 1.1E-04 | 0.0011 | 0.15 | 4.0E-04 | 0.0054 | 0.33 | 7.0E-05 | 0.0022 |
| rs10422347 | hsa-miR-4745-5p | 5-trim | 1 | -4 | 0.15 | 1.3E-04 | 0.0014 | 0.15 | 7.8E-04 | 0.0094 | 0.13 | 0.16 | 0.63 |
| rs10422347 | hsa-miR-4745-5p | 5-ext | 2 | 1 | 0.15 | 2.8E-04 | 0.0029 | 0.14 | 0.0015 | 0.016 | 0.11 | 0.21 | 0.71 |
| rs6413505 | hsa-miR-6886-5p | 5-trim | 2 | -2 | 0.16 | 3.4E-04 | 0.0034 | 0.07 | 0.19 | 0.49 | 0.38 | 1.5E-04 | 0.0036 |
| rs2854001 | hsa-miR-6891-5p | 5-ext | 18 | 1 | -0.16 | 4.0E-04 | 0.0040 | -0.16 | 0.0011 | 0.012 | -0.04 | 0.70 | 0.91 |
| rs74085143 | hsa-miR-4781-3p | 5-sub | 1 | 0 | 0.14 | 4.6E-04 | 0.0045 | 0.11 | 0.020 | 0.13 | 0.26 | 0.0036 | 0.046 |
| rs13186787 | hsa-miR-1294 | 5-trim | 2 | -1 | -0.14 | 4.9E-04 | 0.0047 | -0.16 | 3.8E-04 | 0.0053 | NA | NA | NA |
| rs75715827 | hsa-miR-944 | 5-ext | 8 | 1 | -0.14 | 5.0E-04 | 0.0047 | -0.14 | 0.0013 | 0.014 | NA | NA | NA |
| rs4534339 | hsa-miR-1843 | 5-ext | 1 | 5 | 0.13 | 5.8E-04 | 0.0053 | 0.07 | 0.13 | 0.42 | 0.25 | 0.0034 | 0.044 |
| rs13186787 | hsa-miR-1294 | 5-ext | 3 | 1 | -0.14 | 6.1E-04 | 0.0055 | -0.15 | 7.2E-04 | 0.0087 | NA | NA | NA |
| rs12314280 | hsa-miR-5700 | 5-trim | 2 | -2 | 0.15 | 8.7E-04 | 0.0077 | 0.18 | 4.5E-04 | 0.0059 | 0.04 | 0.68 | 0.91 |
| rs78979347 | hsa-miR-9903 | 5-sub | 2 | 0 | -0.15 | 0.0011 | 0.0092 | -0.17 | 5.8E-04 | 0.0073 | NA | NA | NA |
| rs4534339 | hsa-miR-1843 | 5-trim | 2 | -3 | 0.13 | 0.0013 | 0.012 | 0.06 | 0.18 | 0.48 | 0.25 | 0.0034 | 0.044 |
| rs10422347 | hsa-miR-4745-5p | 5-trim | 6 | -2 | 0.13 | 0.0016 | 0.014 | 0.13 | 0.0034 | 0.032 | 0.05 | 0.55 | 0.87 |
| rs191321849 | hsa-miR-500a-3p | 5-ext | 29 | 1 | 0.12 | 0.0019 | 0.015 | 0.13 | 0.0026 | 0.025 | NA | NA | NA |
| rs191321849 | hsa-miR-500a-3p | 5-trim | 4 | -4 | 0.12 | 0.0025 | 0.020 | 0.12 | 0.0047 | 0.043 | NA | NA | NA |
| rs174561 | hsa-miR-1908-3p | 5-ext | 16 | 1 | -0.12 | 0.0027 | 0.021 | -0.16 | 2.2E-04 | 0.0032 | -0.03 | 0.73 | 0.93 |
| rs75258105 | hsa-miR-5700 | 5-trim | 2 | -2 | 0.14 | 0.0029 | 0.022 | 0.16 | 0.0015 | 0.016 | NA | NA | NA |
| rs515924 | hsa-miR-548al | 5-trim | 1 | -1 | -0.12 | 0.0036 | 0.027 | -0.14 | 0.0027 | 0.026 | -0.07 | 0.48 | 0.87 |
| rs191321849 | hsa-miR-500a-3p | 5-trim | 8 | -1 | 0.11 | 0.0036 | 0.027 | 0.12 | 0.0049 | 0.043 | NA | NA | NA |
| rs6413505 | hsa-miR-6886-5p | 5-trim | 3 | -1 | 0.13 | 0.0052 | 0.036 | 0.06 | 0.26 | 0.56 | 0.32 | 0.0014 | 0.019 |
| rs78979347 | hsa-miR-9903 | 5-trim | 2 | -1 | -0.12 | 0.0055 | 0.037 | -0.15 | 0.0018 | 0.019 | NA | NA | NA |
| rs13186787 | hsa-miR-1294 | 5-ext | 2 | 3 | -0.11 | 0.0069 | 0.044 | -0.13 | 0.0048 | 0.043 | NA | NA | NA |

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