

# Genetic regulation of human isomiR biogenesis

Guanglong Jiang<sup>1,2</sup>, Jill L. Reiter<sup>2</sup>, Chuanpeng Dong<sup>3</sup>, Yue Wang<sup>2</sup>, Fang Fang<sup>2</sup>, Zhaoyang Jiang<sup>4</sup>, Yunlong Liu<sup>1,2,\*</sup>

<sup>1</sup> Department of BioHealth Informatics, Indiana University Luddy School of Informatics, Computing and Engineering, Indianapolis, IN 46202, USA

<sup>2</sup> Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, IN 46202, USA

<sup>3</sup> Department of Genetics, Yale University, New Haven, CT 06510, USA

<sup>4</sup> Department of Computer Science, Purdue University, West Lafayette, IN 47907, USA

\* Correspondence: yunliu@iu.edu; Tel.: +1-317-278-9222

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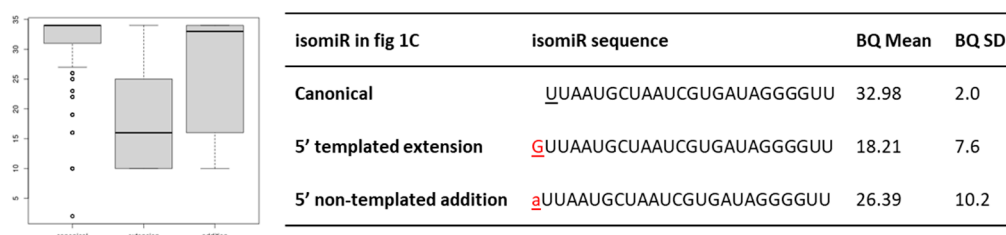


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## Supplementary Materials:

**Supplemental Figure S1.** The boxplot and statistics (mean and standard deviation, SD) of the base quality (BQ) for the first nucleotide at the 5'-end of the hsa-miR-155-5p canonical, 5'-templated extension, and 5'-non-templated addition isomiRs across all study samples.



**Supplemental Figure S2.** Scatter plot of the first two principal components for 1000 Genomes Project subjects. Subjects included in this study are highlighted in colors.

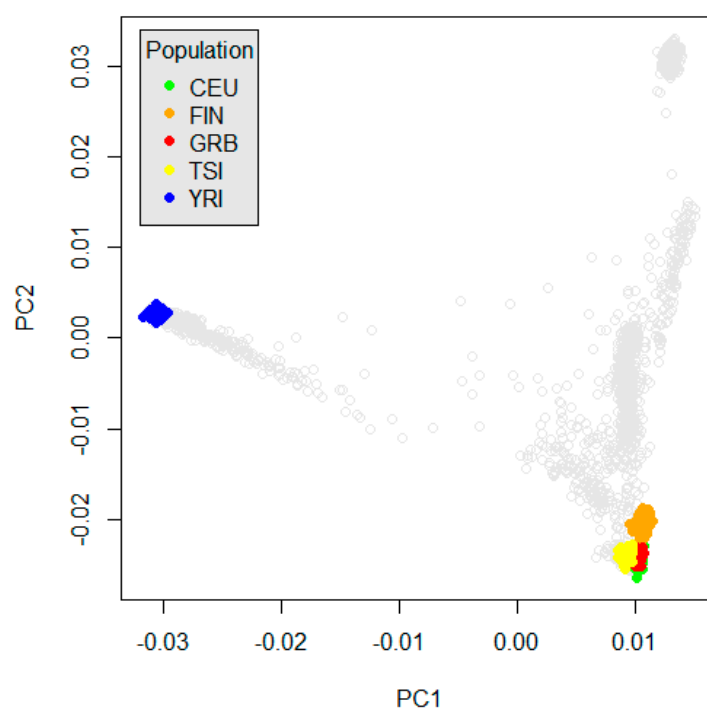
CEU: Utah residents with Northern and Western European Ancestry, European Ancestry

FIN: Finnish in Finland, European Ancestry

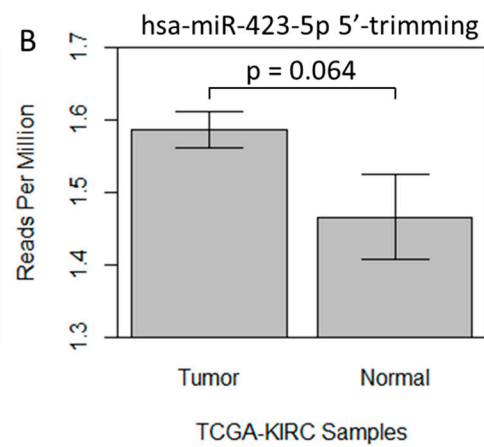
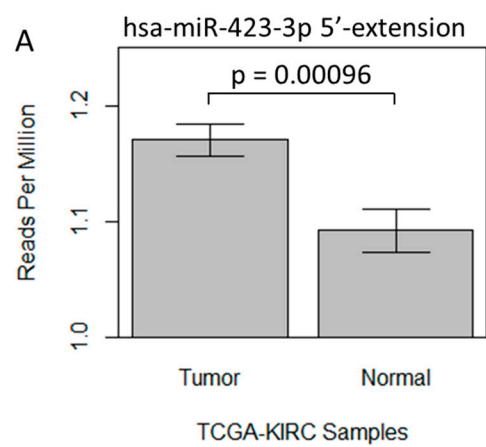
GRB: British in England and Scotland, European Ancestry

TSI: Toscani in Italy, European Ancestry

YRI: Yoruba in Ibadan, Nigeria, African Ancestry



**Supplemental Figure S3.** 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.



**Supplemental Table S1.** Correlation results between SNPs and isomiR compositions 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-548a1	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