

Table SI. Manufacturer information on the miRCURY LNA™ miRNA PCR assays used to quantify candidate miRNAs by digital PCR.

miRNA ID	Genomic location (GRCh38/hg38)	miRBase accession no.	Sense miRBase mature miRNA sequence (5'-3')	Reverse complement miRBase mature miRNA sequence (5'-3')	Catalog no.	GeneGlobe Assay ID
hsa-miR-155-5p	chr21:25,573,980-25,574,044 [+]	MIMAT0000646	UUA AUGCUAAUCGUGAUAGGGGUU	AACCCCUAUCACGAUUAGCAUUA	339306	YP02119311
hsa-miR-183-5p	chr7:129,774,905-129,775,014 [-]	MIMAT0000261	UAUGGCACUGGUAGAAUUCACU	AGUGAAUUCUACCAGUGCCAU	339306	YP00206030
cel-miR-39-3p	NA	MIMAT0000010	UCACCGGGUGUAAAUCAGCUUG	CAAGCUGAUUUACACCCGGUGA	339306	YP00203952

The pre-designed miRCURY LNA™ miRNA PCR assays are manufactured and web lab verified by Qiagen, Inc. The primers sequences used in the pre-designed miRCURY LNA™ miRNA PCR assays are proprietary and not disclosed by the manufacturer (Qiagen, Inc.). Detailed information on each assay can be found at <https://geneglobe.qiagen.com/us/product-groups/mircury-lna-mirna-pcr-assays>. The antisense sequence was generated directly as the reverse complementary sequence of the mature miRNA sequence. NA, not applicable; miRNA/miR, microRNA.

Table SII. Thermocycling conditions used for digital PCR quantifications.

Step	Temperature (°C)	Time (min)
Enzyme activation	95	2:00
Cycling (40 cycles)		
Denaturation	95	0:15
Annealing/Extension	60	1:00
Cooling	35	5:00

Thermocycling conditions used for digital PCR quantification on the QIAcuity One 5-Plex instrument (Qiagen, Inc.).

Table SIII. Characteristics of the study participants from the Gen3G cohort selected for the dPCR validation analysis (n=201).

Characteristics	Value	Range
Mothers		
Age at first trimester, years	28.5±4.0	18.0-47.0
No. of pregnancies carried to term	0.7±0.8	0.0-3.0
Gestational age at delivery, weeks	39.3±1.2	34.2-41.5
Mode of delivery, n (%) vaginal birth	164 (81.6%)	
Newborn		
Sex, n (%) female	99 (49.3%)	
Height, cm	51.1±2.4	43.0-58.5
Weight, g	3,429.6±457.7	2,070.0-5,130.0
UCP leptin level, pg/ml,	16,586.7±16,086.3	1,295.0-87,394.0

Data are presented as mean ± SD or n (%). UCP, umbilical cord plasma.

Table SIV. Variables included in the stepwise linear regression model.

Category	Variable
Outcome	Natural log-transformed leptinemia in UCP (pg/ml)
Maternal characteristics	Maternal age in first trimester (years)
Newborn characteristics	Child's sex (Reference : Male)
Newborn characteristics	Birth weight (g)
Newborn characteristics	Birth length (cm)
Newborn characteristics	Gestational age at birth (years)
Delivery characteristics	Mode of delivery (Vaginal or C-section)
Candidate miRNAs	hsa-miR-518a-5p/hsa-miR-527 (normalized read counts)
Candidate miRNAs	hsa-miR-3909 (normalized read counts)
Candidate miRNAs	hsa-miR-515-3p (normalized read counts)
Candidate miRNAs	hsa-miR-34c-5p (normalized read counts)
Candidate miRNAs	hsa-miR-561-5p (normalized read counts)
Candidate miRNAs	hsa-miR-155-5p (normalized read counts)
Candidate miRNAs	hsa-miR-424-3p (normalized read counts)
Candidate miRNAs	hsa-miR-183-5p (normalized read counts)
Candidate miRNAs	hsa-miR-185-5p (normalized read counts)
Candidate miRNAs	hsa-miR-365a-3p / hsa-miR-365b-3p (normalized read counts)
Candidate miRNAs	hsa-miR-1294 (normalized read counts)
Candidate miRNAs	hsa-miR-192-5p (normalized read counts)
Candidate miRNAs	hsa-miR-339-3p (normalized read counts)
Candidate miRNAs	hsa-miR-3187-3p (normalized read counts)
Candidate miRNAs	hsa-miR-371a-5p (normalized read counts)
Candidate miRNAs	hsa-miR-182-5p (normalized read counts)

Variables entered into the stepwise linear regression model used to identify factors associated with the dependent variable, log-transformed leptinemia in UCP. The model included the 16 candidate miRNAs identified from the DESeq2 analysis (mean normalized read counts >20 and P<0.01), together with maternal and newborn covariates. Variables retained in the final model are presented in Table III. UCP, umbilical cord plasma.

Table SV. 73 miRNAs identified as nominally associated with UCP leptinemia with DESeq2.

miRNAs	Mean normalized read counts	Fold-change	P-value
hsa-miR-3909	123.7	1.14	0.0002
hsa-miR-183-5p	251.4	1.16	0.001
hsa-miR-185-5p	1713	1.21	0.001
hsa-miR-3180 hsa-miR-3180-3p	18.7	1.24	0.001
hsa-miR-34c-5p	24.7	1.28	0.001
hsa-miR-521	2.3	1.69	0.001
hsa-miR-515-3p	23.3	1.25	0.001
hsa-miR-518a-5p hsa-miR-527	74.1	1.27	0.001
hsa-miR-7151-3p	3.9	0.75	0.002
hsa-miR-548i	2.2	1.46	0.003
hsa-miR-424-3p	2839.9	1.10	0.003
hsa-miR-182-5p	5638.7	1.12	0.004
hsa-miR-561-5p	132	1.15	0.004
hsa-miR-1294	391.9	1.15	0.004
hsa-miR-155-5p	876.9	0.91	0.005
hsa-miR-192-5p	97037.7	1.11	0.006
hsa-miR-518d-3p	3	1.41	0.006
hsa-miR-365a-3p hsa-miR-365b-3p	35.3	1.16	0.006
hsa-miR-4443	11.3	1.19	0.008
hsa-miR-339-3p	635.9	0.94	0.008
hsa-miR-3140-3p	1.6	0.69	0.008
hsa-miR-3200-5p	3.3	1.33	0.008
hsa-miR-615-5p	1.7	0.65	0.009
hsa-miR-3187-3p	20.7	1.13	0.01
hsa-miR-371a-5p	61.5	1.22	0.01
hsa-miR-365a-5p	2.2	1.43	0.01
hsa-miR-5000-3p	7	1.17	0.01
hsa-miR-34c-3p	1	1.72	0.01
hsa-miR-628-3p	114.8	0.92	0.01
hsa-miR-412-5p	138.2	0.84	0.02
hsa-miR-219a-5p	6.4	0.84	0.02
hsa-miR-6786-3p	1.4	1.39	0.02
hsa-miR-181a-3p	725.6	0.92	0.02
hsa-miR-345-5p	3071.5	1.06	0.02
hsa-miR-7155-3p	7.8	1.19	0.02
hsa-miR-133b	2.4	1.33	0.02
hsa-miR-3677-3p	40.2	1.10	0.02
hsa-miR-100-5p	914.2	1.15	0.02
hsa-miR-505-5p	15.4	1.11	0.02
hsa-miR-4523	4.8	0.82	0.02
hsa-miR-4482-3p	29.6	1.27	0.02
hsa-miR-19a-3p	3999.7	1.07	0.02
hsa-miR-3617-5p	1.7	0.74	0.03
hsa-miR-4466	19.2	1.11	0.03
hsa-miR-2355-5p	63.4	0.13	0.03
hsa-miR-548at-3p	0.7	1.48	0.03
hsa-miR-409-5p	55.1	0.84	0.03
hsa-miR-550a-3-5p hsa-miR-550a-5p	271	1.08	0.03
hsa-miR-93-5p	37653	1.07	0.03
hsa-miR-25-5p	548.2	1.09	0.03
hsa-miR-503-5p	128.7	1.08	0.03
hsa-miR-548ah-3p hsa-miR-548av-3p hsa-miR-548p	1.2	0.73	0.03
hsa-miR-22-5p	154.3	1.06	0.03
hsa-miR-342-3p	942.2	0.93	0.03
hsa-miR-520f-3p	8.3	1.29	0.03
hsa-miR-181d-5p	564.2	0.94	0.03
hsa-miR-329-5p	29.1	0.88	0.03
hsa-miR-3691-5p	22.6	1.10	0.03
hsa-miR-217	5.2	1.30	0.03
hsa-miR-181c-3p	472.2	0.93	0.04
hsa-miR-3133	1.7	1.32	0.04
hsa-miR-34a-5p	42.9	1.09	0.04
hsa-miR-127-5p	221.7	0.93	0.04
hsa-miR-28-5p	1144.5	0.93	0.04
hsa-miR-4757-5p	0.5	1.52	0.04
hsa-miR-758-3p	190.2	0.90	0.04
hsa-miR-493-3p	902.9	0.93	0.04
hsa-miR-3190-3p	2.2	0.78	0.04
hsa-miR-3200-3p	18.8	1.14	0.04
hsa-miR-202-3p	106	0.82	0.04
hsa-miR-365b-5p	8.5	1.17	0.04
hsa-miR-6791-3p	6.4	0.85	0.04
hsa-miR-339-5p	553.4	0.93	0.04

Associations between miRNA abundance and leptin levels in UCP were assessed using the Wald test integrated into the DESeq2 R package. The model was adjusted for the sequencing batch effect (run and region), the hemolysis degree of UCP samples, the maternal age at the first trimester, the number of pregnancies carried to term, the mode of delivery, the child's sex and the gestational age. Effect sizes of the associations are represented by the fold change values; these are defined as the change in miRNA abundance (mean normalized counts; sequencing counts normalized using the DESeq2 median-of-ratios method) per one unit increase in ln transformed leptin levels in UCP. NGS, Next Generation Sequencing; SD, standard deviation; UCP, umbilical cord plasma.