

Supplementary Information

Supplementary Table 1. Demographics for small RNA-sequencing subset

	NHB (N=36)	NHW (N=41)	
Maternal	mean ± SD	mean ± SD	<i>P-value</i>
Age (years)	26 ± 4	30 ± 6	0.001
Pre-gravid BMI (Lean/Obese) ^β	17/19	22/19	0.737
Net Gestational Weight gain (kg)	9.7 ± 8	12.3 ± 7	0.154
Gestational Weight gain (kg)	13.4 ± 8	16.2 ± 7	0.120
Smoking (N/Y) ^β	29/7	35/6	0.796
Neonatal			
Gestational Age (wks)	39 ± 0.7	39 ± 0.5	0.480
Placenta weight (g)	612 ± 162	681 ± 213	0.113
Birth weight (kg)	3.2 ± 0.5	3.4 ± 0.6	0.115
Placenta efficiency ^γ	5.2 ± 0.9	5.2 ± 0.9	0.821
Length (cm)	49 ± 2	49 ± 2	0.195
Sex (M/F) ^β	21/15	20/21	0.542

Values are mean ± standard deviation. ^γPlacenta efficiency: Birth weight(g)/Placenta weight(g). *P-values* calculated by Student's t-test. ^β*P-value*. Calculated by Chi-squared test.

Supplementary Table 2. Placental miRNA differentially expressed (DE) between NHB and NHW women based on small RNA-sequencing

DE miRNA ↑ in placentas of NHB vs NHW women			DE miRNA ↓ in placentas of NHB vs NHW women		
miRNAs	<i>P-value</i>	<i>Adj. P-value</i>	miRNAs	<i>P-value</i>	<i>Adj. P-value</i>
hsa-miR-6826-3p	7.59E-05	0.005787	hsa-miR-9-3p	0.0005	0.0299
hsa-miR-346	0.000417	0.025004	hsa-miR-217	9.15E-06	0.0010
hsa-miR-1307-5p	0.000976	0.044862	hsa-miR-216a-3p	0.0009	0.0448
hsa-miR-4482-3p	6.37E-10	5.34E-07	hsa-miR-216a-5p	4.05E-05	0.0033
hsa-miR-4482-5p	2.60E-07	6.23E-05	hsa-miR-3129-5p	8.81E-05	0.0064
hsa-miR-1304-3p	5.68E-06	0.000733	hsa-miR-2115-3p	0.0009	0.0448
hsa-miR-34b-5p	7.12E-07	0.000119	hsa-miR-2115-5p	1.06E-05	0.0011
hsa-miR-34b-3p	2.27E-08	9.51E-06	hsa-miR-9-3p	0.0005	0.0299
hsa-miR-34c-5p	1.32E-12	2.21E-09	hsa-miR-146a-5p	3.34E-05	0.0029
hsa-miR-34c-3p	5.31E-07	9.90E-05	hsa-miR-7-5p	0.0004	0.0278
hsa-miR-181c-5p	1.32E-07	3.68E-05	hsa-miR-6877-5p	0.0009	0.0448
hsa-miR-181c-3p	1.63E-08	9.10E-06	hsa-miR-5699-3p	0.0002	0.0157
hsa-miR-181d-5p	0.000781	0.040925	hsa-miR-548f-5p	0.0008	0.0420
hsa-miR-301b-3p	2.23E-05	0.002077	hsa-miR-192-5p	1.18E-05	0.0012
hsa-miR-664b-3p	9.65E-05	0.006745	hsa-miR-3664-3p	3.45E-06	0.0004
			hsa-miR-147b	7.63E-08	2.56E-05
			hsa-miR-3529-3p	0.0004	0.0278
			hsa-miR-7-5p	0.0004	0.0278
			hsa-miR-9-3p	0.0005	0.0299
			hsa-miR-7-5p	0.0004	0.0278
			hsa-miR-941	0.0010	0.0448
			hsa-miR-155-5p	1.47E-05	0.0014
			hsa-miR-223-5p	3.2E-07	6.71E-05
			hsa-miR-223-3p	1.97E-06	0.0003
			hsa-miR-505-3p	0.0003	0.0189
			hsa-miR-505-5p	0.0010	0.0448
			hsa-miR-508-3p	0.0001	0.0086
			hsa-miR-514a-3p	6.37E-05	0.0050

Supplementary Table 3. Results from miRNet 2.0 – a miRNA-centric network visual analytics platform (186 unique genes for placental miRNA highly expressed in non-Hispanic Black women)

Placental derived miRNA	Targeted Genes
hsa-miR-34c-5p	BCL2, GIGYF1, BAZ2A, CDK4, CDK6, HSPA1B, NFE2L1, SRSF2, TGFBR2, YY1, ARHGAP1, CCL22, CNOT4, DDX19B, GXYLT2, IFNLR1, IL6R, KBTBD6, LDHA, MAST3, MET, MLLT1, MRNIP, MYC, MYCN, POTES, SHMT1, SHOC2, SLC35G2, RPA2
hsa-miR-34c-3p	REEP5, XIAP, PHF12, RCOR1, REL, SYNM
hsa-miR-34b-3p	BCL2, CDK4, CDK6, DYNC1LI2, HSPA1B, REEP5, XIAP, YY1, ZNF417, ARHGAP1, CAMSAP2, CHD9, CLCC1, CREB1, GXYLT2, IL6R, LDHA, MAPK14, MET, MRNIP, MYC, MYCN, SHMT1, SRSF7, SYNM, ZNF699
hsa-miR-34b-5p	BCL2, GIGYF1, BAZ2A, CDK4, CDK6, NFE2L1, SRSF2, TGFBR2, XIAP, CNOT4, CREB1, GXYLT2, IFNLR1, MAST3, MET, MLLT1, MYC, MYCN, RHOG, TROVE2
hsa-miR-181d-5p	BCL2, GIGYF1, BAZ2A, DYNC1LI2, HSPA1B, KLHL15, LBR, LDLR, RAN, TNRC6B, ZNF107, BMPR2, CADPS2, CAPRIN2, CCL22, CHD9, CLCC1, DCBLD2, EFCAB14, EN2, ETS1, G3BP2, GK5, GSKIP, KDM5A, LCLAT1, MIGA2, NAA50, NCAPG, NR6A1, PARD6B, PNKD, RCOR1, RHOG, RLIM, RSBN1L, RSF1, SHOC2, SLC35G2, SMCR8, TBL1XR1, TLDC1, TMEM30A, ZBTB4, ZNF268, ZNF439, ZNF487, ZNF556, ZNF616, ZNF699, ZNF829
hsa-miR-181c-5p	BCL2, GIGYF1, BAZ2A, DYNC1LI2, KLHL15, LBR, LDLR, RAN, TGFBR2, TNRC6B, ZNF107, BMPR2, CADPS2, CAPRIN2, CCL22, CHD9, CLCC1, DCBLD2, EFCAB14, EN2, ETS1, G3BP2, GK5, GSKIP, KDM5A, LCLAT1, MIGA2, NAA50, NCAPG, NLK, NR6A1, PNKD, POTES, RCOR1, RHOG, RLIM, RSBN1L, RSF1, SHOC2, SLC35G2, SMCR8, TBL1XR1, TLDC1, TMEM30A, ZBTB4, ZNF268, ZNF439, ZNF487, ZNF556, ZNF616, ZNF699, ZNF829
hsa-miR-181c-3p	G3BP2, TBL1XR1
hsa-miR-301b-3p	CDK4, DYNC1LI2, LDLR, NFE2L1, PNRC1, RAN, SRSF2, TGFBR2, TNRC6B, XIAP, YY1, ZNF107, ZNF417, ARHGAP1, CAMSAP2, CAPRIN2, CNOT4, DCBLD2, IFNLR1, KBTBD6, LCLAT1, MIGA2, NAA50, PHF12, RLIM, RNF11, TMEM30A, TROVE2, ZBTB4
hsa-miR-1304-3p	KLHL15, LDLR, PNRC1, REEP5, SRSF2, YY1, ZNF417, BMPR2, DDX19B, GK5, IL6R, KBTBD6, KDM5A, LDHA, MRNIP, NLK, PHF12, POTES, REL, RNF11, RSBN1L, SRSF7, ZNF439, ZNF487, ZNF556, ZNF829
hsa-miR-301b-3p	CDK4, DYNC1LI2, LDLR, NFE2L1, PNRC1, RAN, SRSF2, TGFBR2, TNRC6B, XIAP, YY1, ZNF107, ZNF417, ARHGAP1, CAMSAP2, CAPRIN2, CNOT4, DCBLD2, IFNLR1, KBTBD6, LCLAT1, MIGA2, NAA50, PHF12, RLIM, RNF11, TMEM30A, TROVE2, ZBTB4
hsa-miR-664b-3p	HSPA1B, LBR, PNRC1, RAN, REEP5, ZNF107, CREB1, EN2, GSKIP, MAPK14, NCAPG, NLK, PARD6B, RNF11, SHMT1, SYNM, TLDC1, TROVE2, ZNF616
hsa-miR-346	ACVR2B, BTG2, CAMSAP2, CAND1, CCND2, CD164, CDK6, CELF1, DDX3X, DICER1, LIF, MTPN, NFIA, NFIB, NR6A1, PIK3R3, PNRC1, RAD51AP1, RPA2, SFT2D2, SYNCRIP, SYNM, TCF7L2, TMEM245, TMEM64, UBAP2L, BE2W, UCHL1, ZNF417
hsa-miR-4482-3p	KLHL15, CAMSAP2, MAPK14, MLLT1, PARD6B, RSF1, SRSF7, ZNF268
hsa-miR-4482-5p	CDK6, PNRC1, TNRC6B, DDX19B, REL, SMCR8
hsa-mir-1307-5p	BTG2, DICER1, EDEM3, OGT, RPL37

Supplementary Table 4. Cell signaling pathways targeted by miRNAs highly expressed in placentas of non-Hispanic Black women (Reactome 2020 Database)

Pathway name	Entities <i>P-Value</i>	Entities FDR	Genes
Attenuation phase	3.94E-08	1.88E-05	HSPA1B
HSF1-dependent transactivation	1.81E-07	4.31E-05	HSPA1B
HSF1 activation	5.57E-07	8.81E-05	RPA2;HSPA1B
Regulation of HSF1-mediated heat shock response	1.12E-06	1.34E-04	RPA2;HSPA1B
Cellular response to heat stress	4.13E-06	3.93E-04	RPA2;HSPA1B
Gene expression (Transcription)	8.80E-06	6.95E-04	TCF7L2;BTG2;CBX6;RPA2;BAZ2A;DICER1;SOD2;YY1;NR6A1;CCND2;CDK6;NFIA;RRAGD;CDC27;SRSF2;E2F5;ZNF664;SRSF7;E2F7;DCP2;TNRC6B
RNA Polymerase II Transcription	1.14E-04	0.007	TCF7L2;BTG2;CBX6;RPA2;SOD2;YY1;NR6A1;CCND2;CDK6;RRAGD;CDC27;SRSF2;E2F5;ZNF664;SRSF7;E2F7;DCP2;TNRC6B
Generic Transcription Pathway	2.24E-04	0.013	TCF7L2;BTG2;CBX6;RPA2;SOD2;YY1;NR6A1;CCND2;CDK6;RRAGD;CDC27;E2F5;ZNF664;E2F7;DCP2;TNRC6B
Nuclear Receptor transcription pathway	3.11E-04	0.016	NR6A1
UCH proteinases	5.61E-04	0.025	YY1;UCHL1;INO80D;MBD6;TGFB2
Cellular responses to stress	5.95E-04	0.025	CBX6;CDK6;RRAGD;CDC27;RPA2;RPL37;SOD2;HSPA1B;DCP2;TNRC6B
Cellular responses to stimuli	7.28E-04	0.028	CBX6;CDK6;RRAGD;CDC27;RPA2;RPL37;SOD2;HSPA1B;DCP2;TNRC6B
TP53 Regulates Transcription of Cell Cycle Genes	0.001	0.037	BTG2;E2F7
Interleukin-7 signaling	0.001	0.042	PIK3R3;BRWD1
Regulation of RUNX1 Expression and Activity	0.001	0.042	CCND2;CDK6;TNRC6B
Aberrant regulation of mitotic cell cycle due to RB1 defects	0.001	0.054	CCND2;CDK6;CDC27
SHOC2 M1731 mutant abolishes MRAS complex function	0.002	0.054	PPP1CC;SHOC2
Diseases of mitotic cell cycle	0.002	0.054	CCND2;CDK6;CDC27
RHOV GTPase cycle	0.002	0.054	DST;WASL;SPTBN1
Signaling by MRAS-complex mutants	0.002	0.054	PPP1CC;SHOC2
Gain-of-function MRAS complexes activate RAF signaling	0.002	0.054	PPP1CC;SHOC2
BH3-only proteins associate with and inactivate anti-apoptotic BCL-2 members	0.002	0.054	BCL2
Interleukin-4 and Interleukin-13 signaling	0.003	0.063	BCL2;LIF;MCL1
Global Genome Nucleotide Excision Repair (GG-NER)	0.003	0.068	YY1;INO80D;CDC27;RPA2

Signaling by Interleukins	0.004	0.077	BCL2;LIF;PIK3R3;BRWD1;SOD2;MCL1
Transcriptional Regulation by VENTX	0.004	0.077	TCF7L2;CDC27;TNRC6B
Cyclin D associated events in G1	0.005	0.087	CCND2;CDK6;E2F5
G1 Phase	0.005	0.087	CCND2;CDK6;E2F5
Defective binding of RB1 mutants to E2F1,(E2F2, E2F3)	0.006	0.090	CCND2;CDK6
Aberrant regulation of mitotic G1/S transition in cancer due to RB1 defects	0.006	0.090	CCND2;CDK6
NR1H2 & NR1H3 regulate gene expression linked to lipogenesis	0.006	0.090	SCD
Mitotic G1 phase and G1/S transition	0.006	0.090	CCND2;CDK6;RPA2;E2F5
Removal of the Flap Intermediate	0.006	0.091	CDC27;RPA2
Processive synthesis on the lagging strand	0.007	0.091	CDC27;RPA2
Signaling by TGFB family members	0.007	0.091	PPP1CC;E2F5;ACVR2B;TGFB2
TP53 Regulates Transcription of Genes Involved in G1 Cell Cycle Arrest	0.008	0.098	E2F7
Nucleotide Excision Repair	0.008	0.105	YY1;INO80D;CDC27;RPA2
Removal of the Flap Intermediate from the C-strand	0.009	0.107	CDC27;RPA2
Mismatch repair (MMR) directed by MSH2:MSH3 (MutSbeta)	0.009	0.107	CDC27;RPA2
Mismatch repair (MMR) directed by MSH2:MSH6 (MutSalpha)	0.009	0.107	CDC27;RPA2
PCNA-Dependent Long Patch Base Excision Repair	0.010	0.107	CDC27;RPA2
Mismatch Repair	0.010	0.107	CDC27;RPA2
Nephrin family interactions	0.012	0.122	WASL;SPTBN1
HDR through Homologous Recombination (HRR)	0.013	0.122	RAD51AP1;CDC27;RPA2
TGFBR2 MSI Frameshift Mutants in Cancer	0.013	0.122	TGFBR2
Lagging Strand Synthesis	0.013	0.122	CDC27;RPA2
Gap-filling DNA repair synthesis and ligation in GG-NER	0.014	0.124	CDC27;RPA2
Signaling by Nuclear Receptors	0.015	0.124	YY1;SCD;BCL2;PIK3R3;TNRC6B
Downregulation of TGF-beta receptor signaling	0.015	0.124	PPP1CC;TGFB2
TP53 regulates transcription of additional cell cycle genes whose exact role in the p53 pathway remain uncertain	0.015	0.124	BTG2
DNA Replication	0.015	0.124	CDC27;RPA2
Estrogen-dependent nuclear events downstream of ESR-membrane signaling	0.016	0.124	BCL2
Transcriptional Regulation by TP53	0.017	0.124	BTG2;RRAGD;RPA2;E2F7;DCP2;TNRC6B

Recognition of DNA damage by PCNA-containing replication complex	0.017	0.124	CDC27;RPA2
Neurodegenerative Diseases	0.017	0.124	SOD2
Deregulated CDK5 triggers multiple neurodegenerative pathways in Alzheimer's disease models	0.017	0.124	SOD2
Cell Cycle, Mitotic	0.019	0.124	PPP1CC;CCND2;CDK6;TAOK1;CDC27;RPA2;E2F5
Resolution of AP sites via the multiple-nucleotide patch replacement pathway	0.020	0.124	CDC27;RPA2
Signaling by TCF7L2 mutants	0.020	0.124	TCF7L2
Evasion of Oxidative Stress Induced Senescence Due to Defective p16INK4A binding to CDK4 and CDK6	0.020	0.124	CDK6
Evasion of Oncogene Induced Senescence Due to Defective p16INK4A binding to CDK4 and CDK6	0.020	0.124	CDK6
Evasion of Oxidative Stress Induced Senescence Due to p16INK4A Defects	0.020	0.124	CDK6
Evasion of Oncogene Induced Senescence Due to p16INK4A Defects	0.020	0.124	CDK6
Signaling by TGF-beta Receptor Complex	0.020	0.124	PPP1CC;E2F5;TGFBR2
NR1H2 and NR1H3-mediated signaling	0.020	0.124	SCD;TNRC6B
Estrogen-dependent gene expression	0.020	0.124	YY1;BCL2;TNRC6B
Processive synthesis on the C-strand of the telomere	0.021	0.127	CDC27;RPA2
Termination of translesion DNA synthesis	0.023	0.132	CDC27;RPA2
TGF-beta receptor signaling activates SMADs	0.024	0.132	PPP1CC;TGFBR2
Activation of the pre-replicative complex	0.024	0.132	RPA2
Loss of Function of TGFBR2 in Cancer	0.026	0.132	TGFBR2
TGFBR2 Kinase Domain Mutants in Cancer	0.026	0.132	TGFBR2
TGFBR1 LBD Mutants in Cancer	0.026	0.132	TGFBR2
tRNA-derived small RNA (tsRNA or tRNA-related fragment, tRF) biogenesis	0.026	0.132	DICER1
Diseases of cellular response to stress	0.026	0.132	CDK6
Diseases of Cellular Senescence	0.026	0.132	CDK6
DNA strand elongation	0.027	0.137	CDC27;RPA2
ESR-mediated signaling	0.029	0.149	YY1;BCL2;PIK3R3;TNRC6B
DNA Damage Recognition in GG-NER	0.030	0.151	YY1;INO80D
Dual Incision in GG-NER	0.031	0.158	CDC27;RPA2
RAF activation	0.031	0.158	PPP1CC;SHOC2
Oncogene Induced Senescence	0.033	0.158	CDK6;TNRC6B
The NLRP1 inflammasome	0.033	0.158	BCL2

S Phase	0.033	0.158	CDC27;RPA2;E2F5
Homologous DNA Pairing and Strand Exchange	0.035	0.158	RAD51AP1;RPA2
RHO GTPase cycle	0.035	0.158	DST;SPTBN1
Extra-nuclear estrogen signaling	0.038	0.158	BCL2;PIK3R3
Mitotic Spindle Checkpoint	0.039	0.158	PPP1CC;TAOK1;CDC27
TGFBR1 KD Mutants in Cancer	0.039	0.158	TGFBR2
Hyaluronan biosynthesis and export	0.039	0.158	HAS2
NADE modulates death signalling	0.039	0.158	DCP2
Translesion synthesis by Y family DNA polymerases bypasses lesions on DNA template	0.042	0.168	CDC27;RPA2
Resolution of Abasic Sites (AP sites)	0.042	0.168	CDC27;RPA2
Oxidative Stress Induced Senescence	0.042	0.169	CBX6;CDK6;TNRC6B
FOXO-mediated transcription of oxidative stress, metabolic and neuronal genes	0.043	0.174	SOD2
Loss of Function of TGFBR1 in Cancer	0.046	0.184	TGFBR2
SMAD2/3 Phosphorylation Motif Mutants in Cancer	0.046	0.184	TGFBR2
Post-transcriptional silencing by small RNAs	0.046	0.184	TNRC6B
Deubiquitination	0.046	0.185	YY1;UCHL1;INO80D;MBD6;TGFBR2
Cellular Senescence	0.046	0.187	CBX6;CDK6;CDC27;TNRC6B
Telomere C-strand (Lagging Strand) Synthesis	0.046	0.187	CDC27;RPA2