

Short Communication: Asymmetric Dimethylarginine Impairs Angiogenic Progenitor Cell Function in Patients With Coronary Artery Disease Through a MicroRNA-21 Dependent Mechanism

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Asymmetric Dimethylarginine Impairs Angiogenic Progenitor Cell Function in Patients With Coronary Artery Disease Through a MicroRNA-21–Dependent Mechanism

Felix Fleissner, Virginija Jazbutyte, Jan Fiedler, Shashi K. Gupta, Xiaoke Yin, Qingbo Xu, Paolo Galuppo, Susanne Kneitz, Manuel Mayr, Georg Ertl, Johann Bauersachs, Thomas Thum

Rationale: The endogenous nitric oxide synthase inhibitor asymmetrical dimethylarginine (ADMA) is increased in patients with coronary artery disease and may regulate function of circulating angiogenic progenitor cells (APCs) by small regulatory RNAs.

Objectives: To study the role of microRNAs in ADMA-mediated impairment of APCs.

Methods and Results: By using microarray analyses, we established microRNA expression profiles of human APCs. We used ADMA to induce APC dysfunction and found 16 deregulated microRNAs. We focused on *miR-21*, which was 3-fold upregulated by ADMA treatment. Overexpression of *miR-21* in human APCs impaired migratory capacity. To identify regulated *miR-21* targets, we used proteome analysis, using difference in-gel electrophoresis followed by mass spectrometric analysis of regulated proteins. We found that transfection of *miR-21* precursors significantly repressed superoxide dismutase 2 in APCs, which resulted in increased intracellular reactive oxygen species concentration and impaired nitric oxide bioavailability. *MiR-21* further repressed sprouty-2, leading to Erk Map kinase–dependent reactive oxygen species formation and APC migratory defects. Small interference RNA–mediated superoxide dismutase 2 or sprouty-2 reduction also increased reactive oxygen species formation and impaired APC migratory capacity. ADMA-mediated reactive oxygen species formation and APC dysfunction was rescued by *miR-21* blockade. APCs from patients with coronary artery disease and high ADMA plasma levels displayed >4-fold elevated *miR-21* levels, low superoxide dismutase 2 expression, and impaired migratory capacity, which could be normalized by *miR-21* antagonism.

Conclusions: We identified a novel *miR-21*–dependent mechanism of ADMA-mediated APC dysfunction. *MiR-21* antagonism therefore emerges as an interesting strategy to improve dysfunctional APCs in patients with coronary artery disease. (*Circ Res.* 2010;107:138-143.)

Key Words: endothelial progenitor cells ■ microRNAs ■ ADMA ■ coronary artery disease ■ oxidative stress

The endogenous nitric oxide synthase (NOS) inhibitor asymmetrical dimethylarginine (ADMA) is a major risk factor in patients with coronary artery disease (CAD).^{1–3} Functionally, ADMA induces dysfunction of circulating angiogenic progenitor cells (APCs) (early outgrowth endothelial progenitor cells or circulating angiogenic cells)⁴ and impairs neovascularization⁵ by direct inhibition of the endothelial NOS.⁶ NO plays a crucial role in mobilization, differentiation, and function of APCs,^{7,8} whereas oxidative stress impairs APC function.^{9,10}

MicroRNAs (miRNAs) are a class of highly conserved, noncoding short RNA molecules that regulate a large portion of the genome. MiRNAs play a crucial role in cardiac

biology, and miRNA dysregulation is often found in cardiovascular diseases.¹¹ Knockdown of the miRNA-processing enzyme Dicer in endothelial cells reduces the formation of capillary-like structures by profound dysregulation of angiogenesis-related genes,¹² and Dicer-deficient mice die from impaired blood vessel formation and vascularization.¹³ Recently, miRNAs have been shown to be interesting therapeutic targets in cardiovascular disease, including cardiac fibrosis¹⁴ and postmyocardial remodeling.¹⁵

In this study, we hypothesized that ADMA exerts effects on the miRNA transcriptome in APCs, leading to functional impairment in vitro and in patients with CAD. In addition, we aimed to identify miRNA-regulated targets and to improve

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Non-standard Abbreviations and Acronyms	
APC	angiogenic progenitor cell
ADMA	asymmetric dimethylarginine
CAD	coronary artery disease
miR	microRNA
miRNA	microRNA
NOS	nitric oxide synthase
ROS	reactive oxygen species
siRNA	small interfering RNA
SPRY2	Sprouty2
SOD2	superoxide dismutase type II

APC function by modulation of an miRNA-dependent mechanism.

Methods

We used microarray-based miRNA transcriptome analyses¹⁴ and a proteome approach¹⁶ to identify miRNA-dependent mechanisms underlying ADMA-mediated dysfunction of human APCs. An expanded Methods section is available in the Online Data Supplement at <http://circres.ahajournals.org>.

Results

MicroRNA Expression in Human APCs

To study miRNA expression in human APCs (for characterization, see the Online Data Supplement) a microarray-based approach to screen for the expression of 312 different human miRNAs was used. MiRNAs of the *let-7* family, *miR-21*, *-16*, *-191*, *-223*, *23a*, and *-23b*, were most easily detectable (Online Table I and Figure 1a). The miRNA expression profile of APCs showed a high degree of similarity with that of human umbilical vein endothelial cells and human coronary arterial endothelial cells, although *miR-223* was enriched in APCs, whereas *miR-126* expression was much higher in mature endothelial cells (see Online Table I).

Table. Deregulated miRNAs in APCs by ADMA Treatment

ID	Fold Change	P	Absolute Expression Levels	
			Control	ADMA, 1 μmol/L
Upregulated miRNAs				
hsa_miR_493_3p	2.92	0.022	414.9	1210.1
hsa_miR_363_AS	2.78	0.004	470.5	1308.4
hsa_miR_21	2.70	0.011	22858.9	61755.3
hsa_miR_126_AS	2.03	0.032	423.1	859.8
hsa_miR_132	1.90	0.025	511.5	973.6
hsa_miR_491	1.88	0.043	455.3	854.7
hsa_miR_487a	1.87	0.023	240.3	449.0
hsa_miR_100	1.80	0.048	393.9	711.0
hsa_miR_518f	1.61	0.045	198.3	319.5
hsa_miR_30a_5p	1.57	0.032	1528.4	2403.9
Downregulated miRNAs				
hsa_miR_524	0.52	0.037	763.9	395.9
hsa_miR_379	0.59	0.018	312.2	184.2
hsa_miR_520c	0.58	0.043	563.0	324.0
hsa_miR_302c	0.60	0.028	606.9	362.7
hsa_miR_376a	0.60	0.047	314.3	189.1
hsa_miR_517c	0.64	0.044	522.3	336.0

MicroRNA Expression in ADMA-Induced APC Dysfunction

ADMA mediates APC dysfunction at least in part by impairment of NO bioavailability.⁴ We thus monitored APC function by testing migratory capacity and used ADMA to induce APC dysfunction. ADMA reduced APC migration in a dose-dependent manner (1 to 10 μmol/L, Figure 1b). We used a pathophysiologically relevant concentration of ADMA (1 μmol/L)⁴ and performed miRNA transcriptome analysis before and 24 hours after addition of ADMA. ADMA treatment resulted in significant changes of the miRNA transcriptome in APCs. Ten miRNAs were significantly increased (Table). Importantly, the relatively high baseline expression level of miR-21 was further 2.7-fold increased by

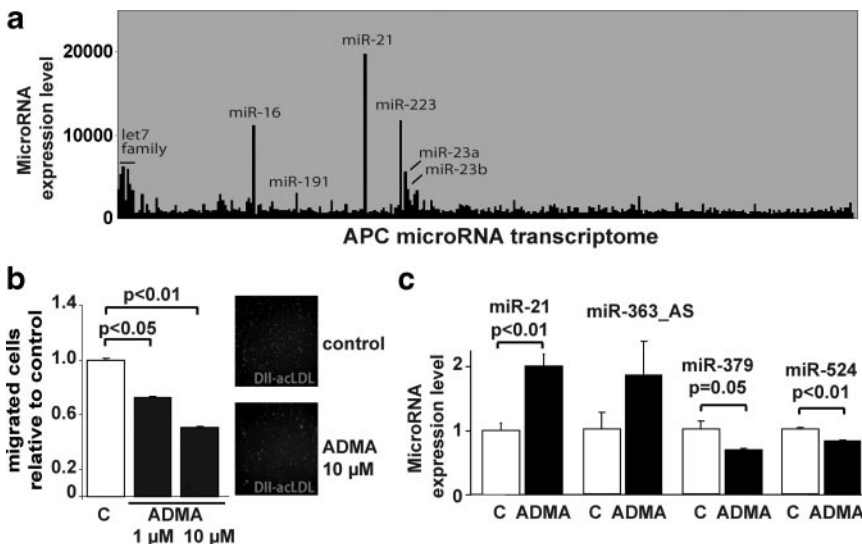


Figure 1. Microarray-based determination of 312 human miRNAs in isolated APCs. **a**, Microarray data are based on n=3 to 4 different donors per cell type. A detailed list of absolute and normalized miRNA expression levels is shown in Online Table I. **b**, Migrated APCs after treatment (24 hours) with different concentrations of ADMA (1 to 10 μmol/L) relative to controls (C). **c**, Real-time PCR-based validation of several miRNAs (in relation to RNU6b) after treatment of APCs with ADMA (1 μmol/L, 24 hours). Data are expressed as means±SEM, n=3 to 4 per experiment/group. The complete data set of ADMA-altered miRNAs is shown in the Table.

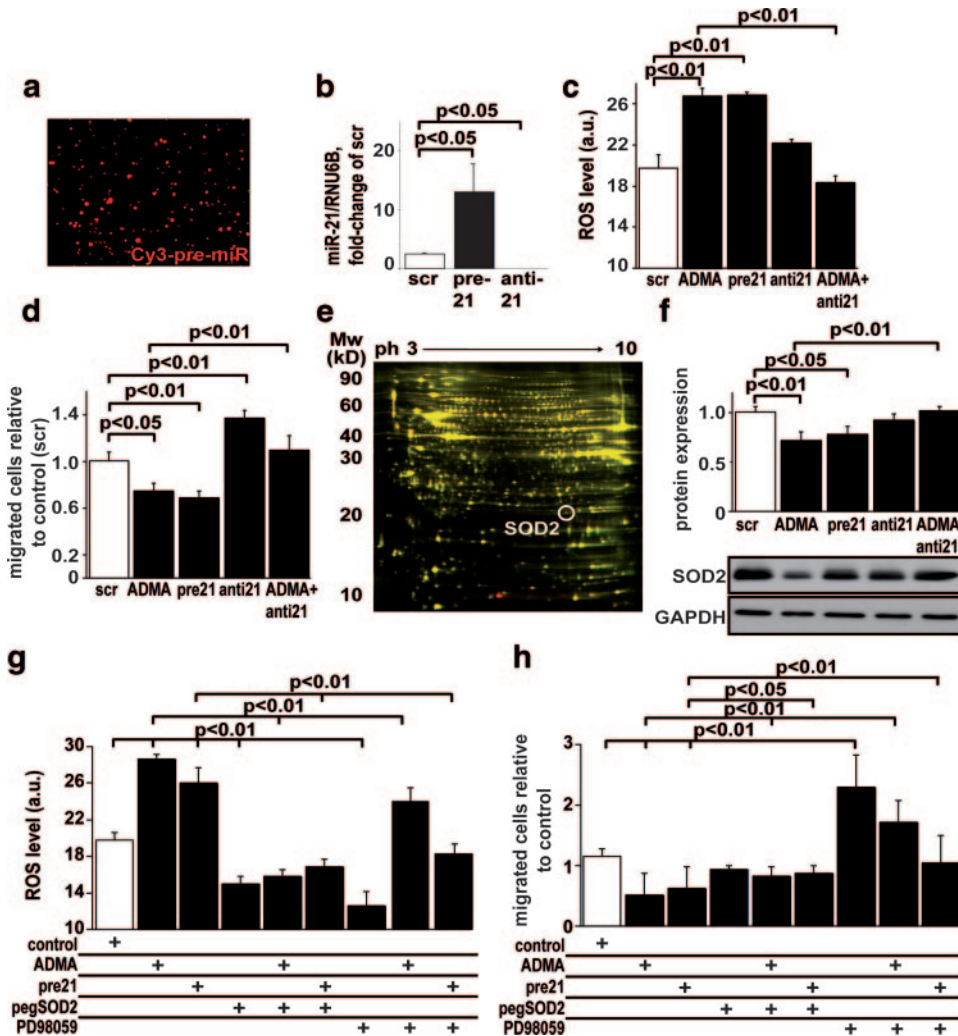


Figure 2. Identification of miR-21 targets in APCs. **a**, Efficient transfection of APCs with Cy3-labeled miRNA precursors to APCs. **b**, miR21/RNU6b levels in APCs 72 hours after transfection with scrambled miRNAs (scr), miR-21 precursors (pre-21), or miR-21 inhibitors (anti-21). **c**, ROS concentration and migratory capacity (**d**) in APCs 72 hours after ADMA treatment and/or miR-21 modulation. **e**, Difference in-gel electrophoresis of human umbilical vein endothelial cells 72 hours after treatment with scrambled miRNAs or miR-21 precursors (each 100 nmol/L). Deregulated SOD2 is highlighted by white circle. A detailed list of regulated proteins is shown in Online Table II. **f**, Protein expression of SOD2 and GAPDH in APCs 72 hours after ADMA treatment and/or miR-21 modulation. Impact of the addition of pegylated SOD2 (pegSOD2) or the Erk Map kinase inhibitor PD98059 on ROS formation (**g**) or migratory capacity (**h**) of APCs. Data are expressed as means \pm SEM, n=3 to 6 per experiment/group.

ADMA treatment. Six miRNAs were significantly repressed by ADMA (Table). Regulation of several miRNAs was validated by miRNA-specific real-time RT-PCR (Figure 1c). We focused our further studies on the role of miR-21 in APC function.

ADMA Increases Reactive Oxygen Species (ROS) Formation, Reduces NO Bioavailability, and Impairs APC Migration by miR-21

To identify miR-21 function in APCs, we transfected miR-21 precursors and inhibitors. Transfection efficiency in APCs and mature endothelial cells was high, based on detection of Cy3-labeled miRNA precursors and increase in miR-21 expression, whereas transfection of miR-21 inhibitors significantly lowered miR-21 expression (Figure 2a and 2b and data not shown). MiR-21 overexpression and ADMA treatment resulted in increased ROS concentration (Figure 2c), reduced NO bioavailability (Online Figure I), and impaired migratory capacity of human APCs, whereas miR-21 inhibition blocked such ADMA-mediated effects (Figure 2c and 2d and Online Figures I and II). There were no significant changes of miR-21 modulation on APC apoptosis (Online Figure III).

MiR-21 Regulates Superoxide Dismutase 2 (SOD2) and the Erk Map Kinase Inhibitor Sprouty2 in APCs

To screen for miR-21 targets, we first used a difference in-gel electrophoresis approach followed by tandem mass spectrometry analysis to search for deregulations in the proteome of human umbilical vein endothelial cells (Figure 2e). MiR-21 overexpression led to altered expression (P<0.05) of 51 proteins 24 hours after treatment (Figure 2e and Online Figure IV and Online Table II). The strongest repression was found for superoxide dismutase type II (SOD2), a protein that is involved in oxidative stress defense. We validated the miR-21-mediated decrease in SOD2 protein expression in cultured APCs by Western blotting (Figure 2f). ADMA also reduced SOD2 protein expression in APCs, which could be blocked by cotransfection with anti-miR-21 (Figure 2f). In addition, SOD2 mRNA expression was repressed by ADMA treatment (Online Figure V). Of note, the 3'UTR of SOD2 displays no miR-21 binding site, based on 3 different bioinformatic prediction tools (PicTar, TargetScan, and miRBase), suggesting an indirect mechanism of action. To study the role of SOD2 in APCs, we treated cells with pegylated SOD2, which resulted in reduced ROS formation and prevention of

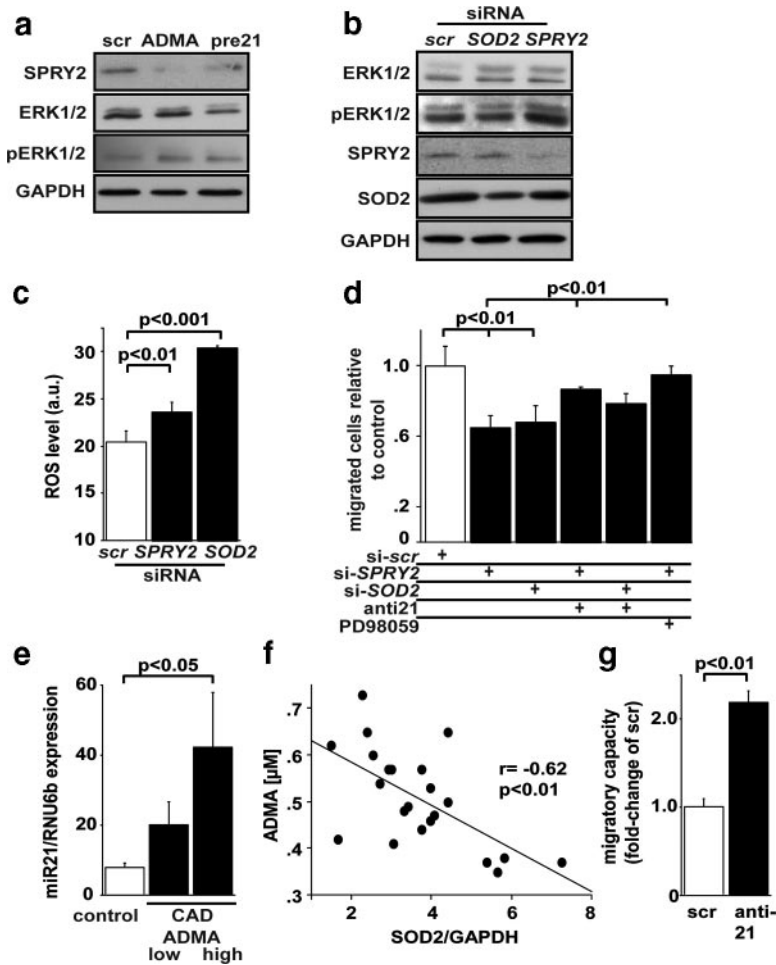


Figure 3. MiR-21-dependent mechanisms leading to APC dysfunction in vitro and in patients with coronary artery disease. **a**, Protein expression of the Erk Map kinase inhibitor SPRY2, ERK1/2, phospho-ERK1/2 (pERK1/2), and GAPDH after treatment of APCs with ADMA (1 $\mu\text{mol/L}$, 24 hours) or transfection with *miR-21* precursors (100 nmol/L, 72 hours). **b**, Protein expression of SPRY2, ERK1/2, pERK1/2, SOD2, and GAPDH after transfection of siRNAs against SOD2 or SPRY2. **c**, ROS formation and migratory capacity (**d**) of APCs transfected with scrambled siRNAs or siRNAs against SPRY1 or SOD2. Additionally, effects of *miR-21* blockade (anti-21) and Erk Map kinase inhibition (PD98059) on migratory capacity are shown. **e**, *miR-21*/RNU6b expression levels in control subjects and patients with CAD and high (>0.55 $\mu\text{mol/L}$) or low (<0.55 $\mu\text{mol/L}$) ADMA plasma levels. Patient information is shown in Online Table III. **f**, Correlation of ADMA plasma levels and SOD2 expression in APCs isolated from patients with CAD. **g**, Migratory capacity of APCs from patients with CAD and high ADMA plasma levels 72 hours after transfection with scrambled (scr) or *miR-21* inhibitors (anti-21). Data are expressed as means \pm SEM, n=3 to 8 per experiment/group.

ADMA-mediated and *miR-21*-mediated ROS increase (Figure 2g) as well as normalization of migratory capacity (Figure 2h). Interestingly, the effects of ADMA and *miR-21* were at least in part dependent on the Erk Map kinase signaling pathway based on inhibition experiments with PD98059 (Figure 2g and 2h). In line, ADMA and *miR-21* decreased the Erk Map kinase inhibitor Sprouty2 (SPRY2), leading to enhanced ERK1/2 phosphorylation (Figure 3a). We next tested whether small interfering (si)RNA-mediated reduction in SOD2 or SPRY2 expression would mimic the effects of *miR-21* (Figure 3b). Of note, SPRY2 reduction by siRNA also resulted in increased ERK1/2 phosphorylation (Figure 3b). Comparable to the effects of *miR-21*, the reduction of SPRY2 or SOD2 increased ROS formation and impaired APC migratory capacity (Figure 3c and 3d). Impaired migration of SPRY2-deficient APCs could be completely normalized by Erk Map kinase inhibition but only partly by cotreatment with anti-*miR-21*. The effect of siRNA-mediated SOD2 reduction on APC migration could not be rescued by *miR-21* blockade (Figure 3d), suggesting important roles of SPRY2 and SOD2 in *miR-21*-mediated APC dysfunction.

MiR-21 Activation in APCs From Patients With CAD

To translate the in vitro findings into a clinical scenario, we isolated APCs from patients with angiographically proven

CAD as well as control subjects (no CAD, see Online Table III) and determined ADMA plasma levels, *miR-21* expression, and APC function. APCs from CAD patients with high ADMA plasma levels showed significantly increased *miR-21* expression levels compared with patients with low ADMA levels or control subjects (Figure 3e). *MiR-21* expression of isolated APCs significantly correlated with ADMA plasma levels ($r=0.57$, $P<0.01$) and inversely with migratory capacity ($r=-0.56$; $P\leq 0.05$). ADMA plasma levels inversely correlated with SOD2 expression in APCs ($r=-0.62$; $P<0.01$; Figure 3f) as determined in a subgroup of an independent study population with CAD.⁴ To study a functional role of increased *miR-21* levels in APC dysfunction of CAD patients, we performed further ex vivo studies. We transfected APCs from CAD patients with *miR-21* inhibitors or scrambled controls and investigated APC migratory capacity. Blockade of *miR-21* by anti-*miR-21* but not by scrambled controls normalized APC function of CAD patients (Figure 3g), identifying *miR-21* as a potential therapeutic target in dysfunctional APCs.

Discussion

ADMA inhibits the enzyme activity of NOSs and contributes to CAD.^{3,6} In this study, we show a further ADMA-mediated mechanism leading to increased oxidative stress and impaired NO bioavailability in APCs, which play a key role in

endothelial regeneration and vascular homeostasis.⁷ We identified *miR-21* to be activated by ADMA and to reduce the expression of superoxide dismutase 2, a key enzyme in oxidative stress defense. In addition, *miR-21* led to oxidative stress by Erk Map kinase activation caused by inhibition of SPRY2. This resulted in impairment of NO availability and APC dysfunction. The in vitro data could be translated into APCs from patients with CAD and high ADMA plasma levels. Treatment with *miR-21* inhibitors rescued APC function in vitro and ex vivo. Recently, a further report found ADMA to result in increased superoxide production in endothelial cells.¹⁷

Because APC dysfunction is mechanistically involved in the onset and progression of endothelial dysfunction and coronary artery disease, specific therapies targeting dysfunctional APCs may be of great clinical value. Indeed, previous studies have suggested that miRNAs may serve as valuable therapeutic targets in a variety of diseases including cardiovascular disease.^{14,15,18,19} For instance, antagonism of *miR-21* has been shown to reduce cardiac fibrosis by a direct effect in cardiac fibroblasts¹⁴ and to prevent vascular neointima proliferation after carotid damage.²⁰ In this study, we show that *miR-21* is also expressed in APCs and that its inhibition reduced ADMA-mediated oxidative stress and improved cellular migratory capacity. *miR-21* thus emerges as an interesting target in various forms of cardiovascular diseases.

Our study has several limitations: we focused only on APCs characterized as described in the Online Data Supplement and thus it remains to be determined whether the *miR-21*-dependent mechanism also contributes to dysfunction of other subtypes of vascular progenitor cells. Also, there may be additional mechanisms involved in how ADMA leads to APC dysfunction, such as endothelial NOS uncoupling²¹ or activation of NADPH oxidases.¹⁷ There are probably many more direct and indirect targets of *miR-21* in APCs that must be uncovered in future studies. However, our data point to a role of *miR-21* in regulation of oxidative stress defense in APCs and identify *miR-21* as a potential therapeutic target in patients with CAD to improve impaired APC function.

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Disclosures

T.T. and J.B. have filed patent applications for the diagnostic and therapeutic use of microRNAs in cardiovascular medicine.

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Novelty and Significance

What Is Known?

- MicroRNAs are regulatory RNA molecules and key players in vascular differentiation and endothelial function.
- Asymmetrical dimethylarginine (ADMA) is an endogenous nitric oxide synthase inhibitor and contributes to endothelial dysfunction and cardiovascular death.
- MicroRNAs emerge as potential powerful therapeutic targets in cardiovascular disease.

What New Information Does This Article Contribute?

- ADMA regulates microRNAs in circulating angiogenic cells.
- ADMA-mediated increase of *miR-21* triggers oxidative stress and dysfunction in circulating angiogenic cells via repression of the Erk Map kinase inhibitor Sprouty-2 and superoxide dismutase 2.
- Targeting *miR-21* rescues ADMA-mediated circulating angiogenic cell dysfunction in vitro and improves functional activity of

proangiogenic cells isolated from patients with coronary artery disease.

ADMA levels are increased in patients with coronary artery disease and contribute to endothelial and angiogenic progenitor cell dysfunction and cardiovascular mortality. MicroRNAs post-transcriptionally regulate about one third of genes and play a major role in endothelial homeostasis and function. We show microRNAs to be altered in dysfunctional angiogenic progenitor cells (circulating angiogenic cells). ADMA increased *miR-21*, which resulted in oxidative stress and dysfunction of angiogenic progenitor cells. *MiR-21* antagonism normalized the function of patient-derived circulating angiogenic cells and may serve as a valuable target for the development of future microRNA-based therapeutic treatment strategies for cardiovascular disease.

Supplement Material

Asymmetric dimethylarginine impairs angiogenic progenitor cell function in patients with coronary artery disease through a microRNA-21 dependent mechanism

Fleissner F, Jazbutyte V, Fiedler J, Gupta S, Yin X, Xu Q, Galuppo P, Kneitz S, Mayr M, Ertl G, Bauersachs J and Thum T

Supplementary Detailed Methods

Isolation, characterization and culture of angiogenic progenitor cells (APC) and endothelial cells

We isolated angiogenic progenitor cells (APC) from healthy volunteers or coronary artery disease patients as described¹. Briefly, peripheral blood mononuclear cells (PBMCs) were isolated by placing whole blood samples on Ficoll® tubes (Amersham) with subsequent centrifugation at 2100 rpm for 20 min. The supernatant was then removed and the interphase was resuspended in 10 ml phosphate buffered saline (PBS) with 2 mM ethylenediaminetetraacetic acid (EDTA). Again, cells were centrifuged at 1200 rpm, supernatant removed and the cell pellet containing PBMCs was seeded on fibronectin coated 6-wells in EBM-2 culture medium supplemented with EGM SingleQuots (Cambrex, UK) and 20% fetal calf serum (FCS) for 4 days. To exclude contamination with mature circulating endothelial cells, we carefully removed culture supernatants 2h after initial seeding and placed non-adherent cells to new fibronectin-precoated wells. This procedure leads to peripheral-blood derived cells with angiogenic properties. Classification schemes and nomenclature of such cells varies in the literature. Most groups name those cells as “early outgrowth EPC”, “EPC”, “monocytic EPC”, “circulating angiogenic cells (CAC)” or “APC”. APC were characterized by cellular uptake of acetylated LDL (dil-acLDL; Molecular Probes, Eugene, USA), binding of fluorescein isothiocyanate (FITC)-conjugated lectin from *Ulex europeus* (UEA-1; Sigma, Germany), expression of vascular endothelial growth factor receptor-2 (VEGFR-2), von Willbrand factor (vWF) and endothelial nitric oxide synthase (eNOS), capacity for integration during endothelial tube formation, cellular migration and colony forming unit (CFU) capacity, as described by us previously¹⁻³. Human umbilical vein endothelial cells (HUVECs) and human coronary arterial endothelial cells (HCAECs) were obtained from Lonza (Germany) and cultured until subconfluence before use.

Cellular migration assays

Modified Boyden chamber assays

Migratory capacity of APC was investigated using the modified Boyden chamber assay as described previously¹. In brief, APC (1×10^4) were cultured in inlets (Falcon HTS Fluoro Blok insert, 8- μ m pore size), which were placed in 24-well culture dishes containing endothelial basal medium (Clonetics, Germany) and 50 ng/mL VEGF, and 100 ng/mL stromal cell-derived factor (SDF)-1 to measure APC migratory capacity. After 24h, migrated cells on the bottom of the membrane were stained with dil-acLDL and counted manually using fluorescence based microscopy evaluation¹.

Scratch wound assays

Additionally, migratory capacity of APC was measured by scratch wound assays. APC were cultured in 24-well plates, transfected for 72h with miR-21 precursors or scrambled controls, stained with Dil-acLDL and photographs were taken directly after and 4h after creating a scratch wound in a confluent monolayer with a 10- μ l tip. The width of the wound was measured using AxioVision software (Zeiss, Germany).

RNA isolation

Total RNA (including miRNAs) was isolated using Trizol (Invitrogen, Germany). Briefly, pellets were dissolved in Trizol reagent for five minutes, chloroform was added and centrifuged at 12000 g for 15 min. The supernatant was conveyed and isopropanol added. A centrifugation step followed for 15 min at 12000g after incubation for 10 min. The precipitated RNA was washed in 75% ethanol and dissolved in RNase-free water. For microarrays, RNA was isolated using the *mirVana* miRNA Isolation Kit (Ambion) following the company's protocol.

MiRNA microarrays

After isolation of total RNA we purified miRNAs using the flashPAGE Fractionator system (Ambion) as described by the manufacturer. Capillary electrophoresis (Bioanalyzer 2100; Agilent) was used to assess quality of total RNA and purity of isolated miRNAs. miRNA obtained from 10 μ g total RNA was labeled with the dye Cy3 (Molecular Probes, Carlsbad, Calif) with the use of the *mirVana* miRNA Labeling Kit (Ambion) according to the manufacturer's recommendations. Each target was hybridized to a separate array (n=3-4 for each group: APC, APC treated with ADMA (1 μ M for 24h), HUVECs, HCAECs). Microarrays with a set of 464 miRNAs (*mirVana* miRNA Probe Set, Ambion; including 312 different human miRNAs) were spotted in-house on SCHOTT Nexterion Slide E microarray slides in quadruplicate. The oligonucleotide probes were 42 to 46 nucleotides long and consisted of an 18- to 24-nucleotide segment that targeted a specific known human, mouse, or rat miRNA. A complete listing of the probes in the probe set can be found at www.ambion.com/techlib/resources/miRNA_array/index.html. Slide processing, miRNA purification and enrichment, and labeling were performed according to the Ambion *mirVana* manuals (www.ambion.com/techlib/prot/). Data acquisition was done with the use of ScanAlyze Software (M. Eisen, LBNL). Scanned raw data (see Online Table I left) were normalized using the *vsN* package in R. Each array data was subjected to an affine transformation, then the whole data were transformed by a variance-stabilizing transformation using a *glog* (generalized logarithm) function. *glog* is like the natural logarithm for large values (large compared to the background noise), but is less steep for smaller values. Row data after normalization raised to the power on the base of the natural logarithm are shown on the right of Online Table I. Expression of various miRNAs was validated by specific miRNA stem loop primer reverse transcription followed by TaqMan RT-PCR analyses (see below).

MicroRNA Stem Loop RT-PCR and SYBR Green mRNA RT-PCR

Expression of several miRNAs was validated by quantitative miRNA stem loop RT-PCR technology (TaqMan MicroRNA Assays, Applied Biosystems, Foster City, Calif). All miRNA samples were derived from isolations having the same total RNA concentration. We used highly target-specific stem loop structure and reverse transcription primer, and after reverse transcription used specific TaqMan hybridization probes for miRNA amplification. This allows high specificity for only the mature miRNA target and formation of a reverse transcription primer/mature miRNA

chimera, extending the 5' end of the miRNA. The small RNA molecule U6 small nuclear (RNU6-2 or RNU6b) was amplified as a control.

For detection of SOD2 mRNA expression levels we used a realtime SYBR Green-based approach. In detail, after RNA isolation we performed reverse transcription (iScript cDNA synthesis kit, Bio-Rad, Germany) and then used the iQ SYBR Green Supermix (Bio-Rad, Germany) and the following oligonucleotides for SOD2 amplification: fwd- 5'CAAATTGCTGCTTGTCCTCAA3', rev- 5'TCTCCCAGTTGATTACATTCCA3'. Data were normalized to GAPDH expression.

MiRNA transfection

APC were transfected with precursor and inhibitors of miR-21 (50–100nM, Ambion) using Lipofectamin 2000 (Invitrogen) as described⁴.

Detection of reactive oxygen species (ROS) and nitric oxide (NO) levels in APC

We used a flow cytometry-based method with the substrates dihydroethidium (DHE, 2.5 μ M; Molecular Probes) to detect ROS as described² and diaminofluorescein–2 diacetate (DAF-2/DA) to detect NO levels. For NO detection, we incubated APC (0.5×10^6 cells) for 1h with 10 μ M DAF-2/DA. FACS analysis (FACSCalibur, Becton Dickinson) was performed immediately after trypsinising and suspending the cells in PBS.

Proteome profiling and Western blotting

HUVECs and APCs were treated with miR-21 precursors or scrambled controls (each 100 nM) for 72h before proteome analysis. Key proteomic techniques involved adaptations of previously published protocols, including difference in-gel electrophoresis (DIGE) and tandem mass spectrometry⁵ (see below). Protein lysates were prepared as described¹. We used primary antibodies against superoxide dismutase 2 (SOD2, ab16956, Abcam, Germany), sprouty-2 (SPRY2, ab50317, Abcam, Germany), ERK1/2 (9102, Cell Signaling, Germany), phospho-ERK1/2 (9101, Cell Signaling, Germany) and glyceraldehyde dehydrogenase (GAPDH, ab8245, Abcam, Germany), as well as appropriate secondary antibodies.

Two dimensional difference gel electrophoresis (2D-DIGE)

Cell monolayers were rinsed thoroughly with cold PBS to remove any serum components. Protein extracts were prepared using a lysis buffer (8M urea, 4% w/v CHAPS, 30mM Tris-Cl, pH 8.5) compatible with DIGE labelling (GE Healthcare). After centrifugation at 13,000 g for 10 min, the supernatant containing soluble proteins was harvested and the protein concentration was determined using a modification of the method described by Bradford⁶. The fluorescence dye labelling reaction was carried out at a dye/protein ratio of 200pmol/50 μ g⁷. After incubation on ice for 30 min, the labelling reaction was stopped by scavenging non-bound dyes with 10mM lysine (L8662, Sigma) for 15 min. For two-dimensional gel electrophoresis, samples were mixed with 2x buffer (8M urea, 4% w/v CHAPS, 2% w/v DTT, 2% v/v Pharmalytes 3-10 for IEF), 50 μ g per sample were diluted in rehydration solution (8M urea, 0.5% w/v CHAPS, 0.2% w/v DTT, and 0.2% v/v Pharmalyte pH 3-10) and loaded on IPG strips (18cm, pH 3-10, nonlinear, GE healthcare). After rehydration overnight, strips were focused at 0.05 mA/IPG strip for 28 kVh at 20°C (IPGphor, GE healthcare). Once IEF was complete the strips were equilibrated in 6M urea containing 30% v/v glycerol, 2% w/v SDS and 0.01% w/v Bromphenol blue, with addition of 1% w/v DTT for 15 min, followed by the same buffer without DTT, but with the addition of 4.8% w/v iodoacetamide for 15 min. SDS-

PAGE was performed using 12% T (total acrylamide concentration), 2.6% C (degree of cross-linking) polyacrylamide gels without a stacking gel, using the Ettan DALT system (GE healthcare). The second dimension was terminated when the Bromophenol blue dye front had migrated off the lower end to the gels. After electrophoresis, fluorescence images were acquired using the Ettan DIGE imager (GE healthcare). Finally, gels were fixed overnight in methanol: acetic acid: water solution (4:1:5 v/v/v). Protein profiles were visualised by silver staining using the Plus one silver staining kit (GE healthcare) with slight modifications⁸ to ensure compatibility with subsequent mass spectrometry analysis. For documentation, silver-stained gels were scanned in transmission scan mode using a calibrated scanner (GS-800, Bio-Rad). DIGE gels were analysed using the Decyder software (Version 6.5, GE healthcare). All 2-DE gels were of high quality in terms of resolution as well as consistency in spot patterns. Spots exhibiting expression change above 1.2 fold between two groups and a statistical difference ($p < 0.05$) were excised for identification. A detailed methodology is available on our website <http://www.vascular-proteomics.com>.

Nano-LC MS/MS

In-gel digestion with trypsin was performed according to published methods⁹ modified for use with an Investigator ProGest (Genomic Solutions) robotic digestion system. Following enzymatic degradation, samples were separated by liquid chromatography on a reverse-phase column (C18 PepMap100, 3 μm , 100 \AA , 25 cm, Dionex) and applied to a LTQ Orbitrap XL mass spectrometer (Thermo Scientific). Spectra were collected from the mass analyzer using full ion scan mode over the m/z range 300-2000. Six dependent MS/MS scans were performed on each ion using dynamic exclusion. Spectra were collected from the Orbitrap mass analyzer using full ion scan mode over the mass-to-charge (m/z) range 450-1800. MS-MS scans were performed on each ion using dynamic exclusion.

Data Analysis of proteome data

Database searches were performed using the TurboSEQUENT software (Bioworks Browser version 3.3.1, Thermo Fisher) against human database (19804 protein entries, UniProtKB Release 13.5, 10-Jun-2008) using following parameters: parent tolerance 1.5 Da, fragment tolerance 1.0 Da, carbamidomethylation of cysteine as fixed modification, oxidation of methionine as variable modification, maximum missed cleavage: 2. Following filter was applied: for charge state 1, $X_{\text{Corr}} > 1.5$; for charge state 2, $X_{\text{Corr}} > 2.0$; for charge state 3, $X_{\text{Corr}} > 2.5$. Search results were loaded into Scaffold software (version 2.0, Proteome Software) and calculated with X!Tandem. Following filters were applied: peptide probability > 95%, protein probability > 99%, minimum No. of peptides per protein: 2.

Study subjects and determination of ADMA plasma levels

Approval from the ethical committee of the University of Würzburg was obtained, as was informed written consent from patients. Patients admitted to hospital because of stable angina with subsequent coronary angiography were enrolled. Only patients with documented coronary artery disease (2- or 3-vessel disease) were included (see also Online Table III for further patient characteristics). APC were isolated and cultured as described above. ADMA plasma levels were determined as described¹⁰.

Statistical analysis

Data are expressed as means \pm SEM. Statistical analysis was performed by one-way

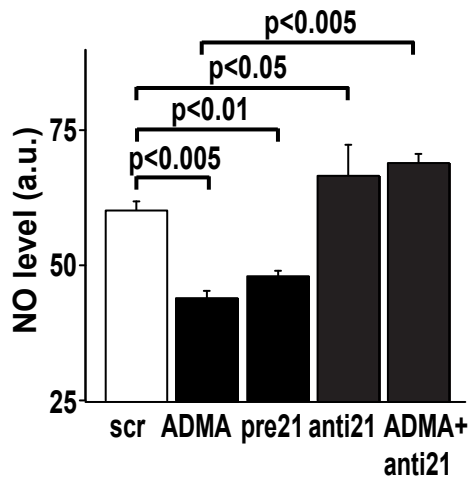
ANOVA followed by multiple comparisons using Fisher's protected least significant difference test. To analyze relationships between variables simple regression analyses were performed. Statistical analysis was performed using StatView 5.0 statistic program (Abacus Concepts, Berkley, CA). Statistical significance was assumed at $P \leq 0.05$.

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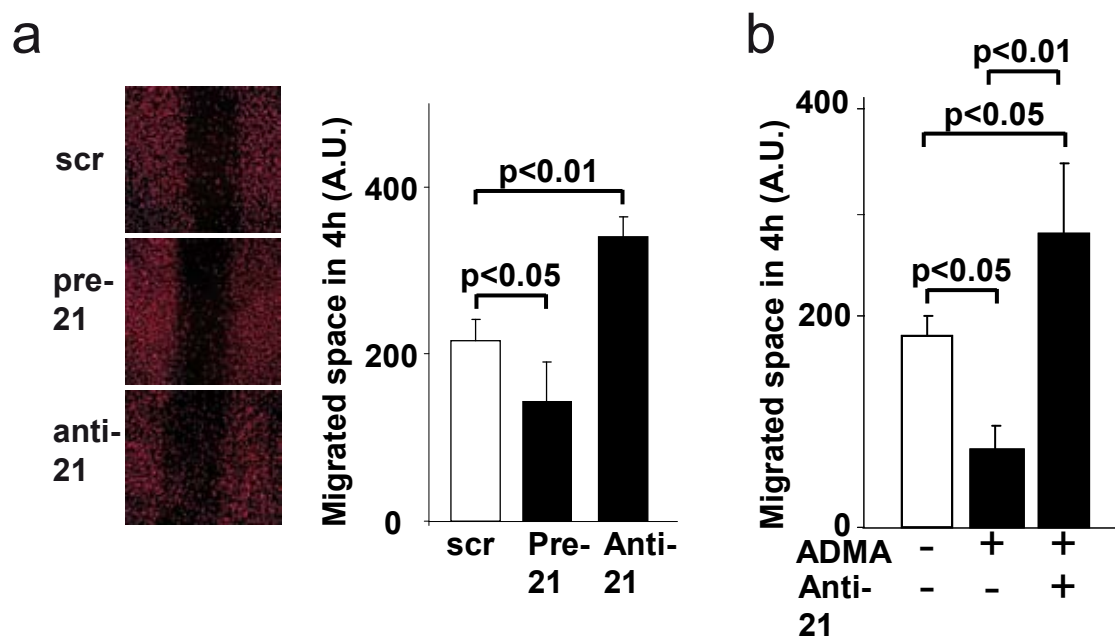
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Online Figure I



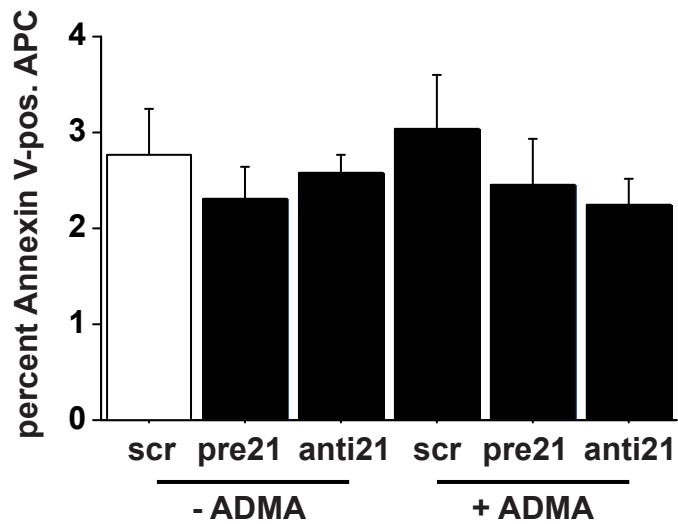
Online Fig. I. NO concentration in APC treated with ADMA, miR-21 precursors (pre-21), anti-miR-21 (anti-21) or controls (scr). Data are mean \pm SEM. n=3-4 per experiment/group

Online Figure II



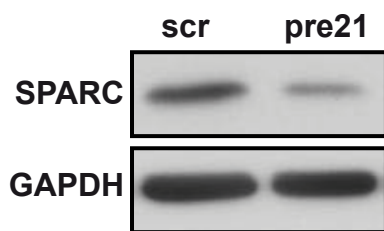
Online Fig. II a,b. Scratch wound assays for determination of migratory capacity of APC treated with ADMA, scrambled miRNAs (scr), miR-21 precursors (pre-21), anti-miR-21 (anti-21) or controls. Data are mean \pm SEM. n=3-4 per experiment/group.

Online Figure III



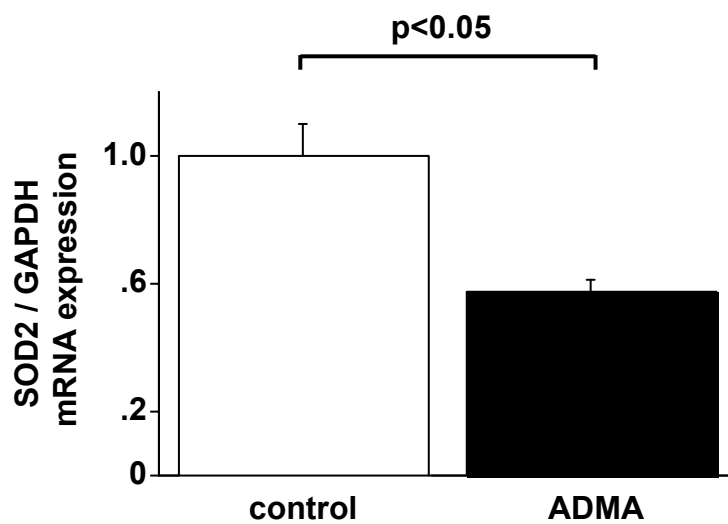
Online Figure III) Percent Annexin V-pos. APC after miR-21 manipulation in the presence or absence of ADMA (1 μ M, 24h). n=4 experiments / group.

Online Figure IV



Online Fig. IV) Protein expression of SPARC in HUVEC after transfection with scrambled miRNA precursors (scr) or miR-21 precursors (pre21).

Online Figure V



Online Fig. V) SOD2 mRNA expression (relative to GAPDH mRNA) in APC treated with or without ADMA (1 μ M, 24h). Data represent mean \pm SEM. n=3 experiments / group.

Online Table I) Absolute and normalized miRNA expression levels in APC, HUVECS and HCAECs

	raw data									
	APC1	APC2	APC3	HUVEC1	HUVEC2	HUVEC3	HCEAC1	HCEAC2	HCEAC3	HCEAC4
hsa_miR_21	13433	15762,5	44427,5	23492,5	21320	58466	40935,5	21257,5	40475	17965
hsa_miR_223	7117	10275	27380	5343	1816,5	1594,5	1382,5	1761	1523	2097,5
hsa_miR_16	5880	9835	27911	8919	12825,5	13909	9456	5567	10110,5	3221,5
hsa_let_7d	3695,5	5888	15748	9117	16407,5	26768,5	14682	19678	50514,5	15376,5
hsa_let_7f	2817	5220	16896	8911	17063	23512	10666	16657,5	31185	9142,5
hsa_miR_23a	3211,5	4377,5	17090	7293	8091	15217	17076,5	7911	9714,5	3567
hsa_let_7c	3097	3797	16954,5	5877,5	9460,5	23275	18744,5	13717,5	21537,5	27154
hsa_let_7g	3104,5	3645	11172,5	6307,5	5800	8217,5	4013,5	4658,5	7976,5	3514
hsa_miR_23b	2385,5	2234	12565	4196,5	8709	8942	12102	6840	11348	2628
hsa_let_7b	2155,5	3078,5	10919,5	5114,5	11141	13000	9789	13098,5	26656,5	18149
hsa_miR_27a	2736	3626	8305	7638	5796,5	9903	3979	6505	6079	5204,5
hsa_miR_191	2459	2571	9346,5	3768	4050,5	4632,5	3575,5	4110,5	8015	4560
hsa_let_7i	3574	3453,5	6762,5	5802,5	6313	11807	4017,5	4664,5	6627	3232
hsa_miR_146a	2835,5	2279,5	8424,5	3230	2763	3548,5	2479	2383,5	3230,5	2109,5
hsa_miR_103	2392	2798	8205	3720,5	4248	3945	3695,5	3163	4611,5	2629,5
hsa_miR_26b	2285,5	2864	7903	3966	3633,5	4475	2773,5	2785	3411,5	2052
hsa_miR_15a	2176	2121,5	7708	2990	2109,5	2260,5	1959,5	1974,5	2375	2027
hsa_miR_485_5p	2913	2767	5872	5176	4565,5	7141	2955,5	3357	4005	3078
hsa_miR_24	1774,5	1865,5	7845,5	3831,5	4590	5947,5	7756	3258	6741,5	2175
hsa_miR_122a	2544,5	2789	5988	4196	3795	5794,5	2143	3294,5	3698,5	3144
hsa_miR_29a	2121,5	2250,5	6451,5	6967	7779	8080,5	8329,5	6531,5	11213,5	3101
hsa_let_7e	2281	2181,5	6152	3543,5	4830	9497	4042,5	5015	13001,5	8415
hsa_miR_34a	2995	2250	4969,5	3133	2458	4151,5	2737	2417	4982,5	2622,5
hsa_miR_146b	2525	2180,5	5402	3014,5	1804	2511,5	1458	1634	2665	2021,5
hsa_miR_19b	1925	2805	5288	4997	4371	6242	2960	3328,5	2793	3717,5
hsa_miR_296	1978	2865,5	5045,5	3911	2841,5	4888,5	2049	2526,5	2735	4364,5
hsa_miR_150	2537	2348	4813	3455,5	1763,5	2212	1451	1565	2644	1862
hsa_miR_155	2092	2388,5	4959	4214,5	5260	6761,5	4518,5	3770	6071,5	3751,5
hsa_miR_519b	2040	1660	5714	2547	2352	3068	2660,5	2178,5	7480	2018
hsa_miR_15b	1744,5	2134,5	5434	2989,5	4284	5232,5	3087	2450	2765	1858
hsa_miR_183	2685	2087,5	4537,5	2829	2245	3472	1781,5	2324	2889,5	2360
hsa_miR_145	2268,5	2342	4679	3644	3156	4054,5	2121	3522,5	2573,5	2419

hsa_miR_106a	1600	1932	5751	4094	4139	4772,5	2657,5	2220,5	3694	2394
hsa_miR_22	2025	1597	5571	2569	2090,5	2912,5	3205,5	2026	4538	2745
hsa_miR_499	2072	2235	4641	3091	2670	4062,5	1938	2225	2868	2138,5
hsa_miR_99a	2900	1825,5	4165	4041,5	5953,5	7737	6165	5002,5	8876	2847
hsa_miR_202_AS	2147,5	2042,5	4425,5	3272	2922	3668	2068,5	2978	2593	2570
hsa_miR_140	2068,5	2288	4147	3720	2606	3483	1981,5	1967,5	4367	2291,5
hsa_miR_30a_5p	2119,5	2195	4130	4060	4020	5176,5	3949,5	3102,5	4706,5	2245
hsa_miR_181b	2353	2011	3983,5	3127,5	2666	3549,5	2997	1949	3556	2555
hsa_miR_30d	1834,5	1770	4708	3206,5	3294,5	3283	4030,5	2472,5	4391	2441
hsa_miR_511	2510	1869	3917	2746	1926	2840	1604,5	1847	2110	2033
hsa_miR_17_5p	2462,5	1584,5	4213	3115	3433,5	4504,5	2687,5	2143	4906	2409
hsa_miR_374	1807,5	2248	4182	4124	3050,5	4211,5	2233	2776,5	5295,5	2664
hsa_miR_30b	2379	1443	4198	2147,5	2063	1652	1861	1843	1990,5	1781
hsa_miR_30e_5p	1606	1665	4697,5	3490,5	1114	836	1051	877	1024,5	1337
hsa_miR_425	2487	1971	3371	2801,5	2276,5	2944	1582	2078	2114,5	2096
hsa_miR_338	2063	2071,5	3657	2706	1792,5	2131	1385,5	1514	2563	2098
hsa_miR_25	1683	2121,5	3963,5	3181	2008	5851	2343,5	2020	2600	2221
hsa_miR_483	1758	2598,5	3411	2213	1687,5	1594,5	1315	1614,5	1291	1864
hsa_miR_373	1824,5	1935	3995,5	3210	2810	3635	1950,5	2440	2218	2547
hsa_miR_147	2133,5	1900	3676	2458	1976	2594,5	1433	1946	2464	2171
hsa_miR_30c	1692,5	1618	4385	2503	2653	2585,5	2523,5	1977	2480	1685
hsa_miR_130a	2794,5	1862	2951	2684	2255	3272,5	1767,5	1766	2697,5	1986
hsa_miR_198	2172,5	1829	3554,5	2751	2496,5	2895,5	1687	1855,5	2670,5	1903
hsa_miR_422a	1797,5	1618	4066	2470,5	2001	2579,5	1435	1995	2254,5	1911
hsa_miR_222	2438,5	2003	3007,5	4977,5	6363	11018	9860,5	4813	10191,5	3365
hsa_miR_484	2416	1870,5	3098,5	2928,5	2030	2899,5	1745	1826	1773,5	3210
hsa_miR_373_AS	2755,5	1630	2969,5	3873	2995	2417	1769,5	2660,5	5053	3618
hsa_miR_182_AS	1777	1971	3587,5	3572,5	2463	2823,5	1626	1997,5	2482,5	1934,5
hsa_miR_361	2631,5	1706	2814,5	2604,5	1877	1707	1784,5	1522	3564	2132
hsa_miR_513	1804,5	1683,5	3645,5	2695,5	2168,5	2790	1650	2010	2247	1765,5
hsa_miR_448	1756	1912,5	3443	2767	1067,5	844	957	834,5	924	1235,5
hsa_miR_423	1790,5	1568	3735	2361	2134	2228	1734	2039	2121	2027,5
hsa_miR_29b	2388	1612	3090,5	3337,5	1901	3669	1831,5	1622	3032	2097,5
hsa_miR_7	1905	1833	3351	2730,5	2481	2404,5	1647,5	1807	2099	1993,5
hsa_miR_370	1792,5	1935,5	3341,5	3790,5	2437	3782,5	1779	2118	2406,5	2193,5
hsa_miR_93	1621	1770	3646,5	3790,5	2751,5	3672,5	1975	1678	3921	2101,5

hsa_miR_221	1637	1840	3538,5	5075	8708	11689	8984,5	5756	10126,5	2907
hsa_miR_125a	1315	1843,5	3847	2330	2234	2736	3033	2062	2543,5	2616
hsa_miR_185	1781	1380,5	3757	2194	1737,5	1420	1321,5	1591,5	1791	1986
hsa_miR_33	1772,5	1590,5	3543,5	3004,5	1819	2072,5	1447,5	1991,5	2325	2144
hsa_miR_335	2449	1656,5	2782,5	2596	2586,5	1725	1392	2087	1863,5	2449
hsa_miR_195	2007	1497	3334,5	4664	2566,5	2336	1905	1898,5	2709,5	1740
hsa_miR_98	1821	1602	3408	2288	2432	2841,5	1697,5	1981	3060,5	2171,5
hsa_miR_422b	1531	1663,5	3587	2526	1795	2071,5	1310,5	1518,5	3153,5	1711,5
hsa_miR_383	1776,5	1784	3196,5	3653,5	2310,5	2608	1560	1952	2077	2172
hsa_miR_96	2258	1612	2885,5	3974	1973	3452	1857,5	1589,5	4156,5	3905,5
hsa_miR_515_3p	1663	1714	3350	2540,5	2033	2414,5	1456	1676,5	1977	1772,5
hsa_miR_526b_AS	2287	1636	2746,5	2346	1640,5	1914,5	1300	1532,5	1839,5	1878
hsa_miR_194	2115,5	1586,5	2964	2334	1641	1836,5	1324	1706	1771	1909,5
hsa_miR_378	1740	1733	3173	2430	1838	2251,5	1466	1607,5	2443,5	1927,5
hsa_miR_432	1481	1812	3345,5	2970	2491	2863,5	1801	2552	1971,5	2632,5
hsa_miR_153	2016,5	1575,5	3015,5	2362,5	1997,5	2113	1483	1838	1701	1678
hsa_miR_384	1744,5	1848,5	2974	2858	2259,5	2696,5	1598,5	2471	1774	2025,5
hsa_miR_29c	1427	1384,5	3752,5	2592	2276,5	2367,5	2187,5	1964	4071	1597,5
hsa_miR_342	1397,5	1422	3716	2592,5	1816,5	2008	1643	1573	2044	1748
hsa_miR_501	1851	1741	2905	2434	1920	2207,5	1456	1646	2494,5	1851,5
hsa_miR_525_AS	2294,5	1291,5	2889	2643,5	2398	2232,5	1950,5	2013,5	2814	1640,5
hsa_miR_135b	1620,5	1496,5	3352,5	2406	1778,5	2080,5	1351,5	1765,5	1274,5	1894
hsa_miR_20b	1713	1380	3357,5	2724	3377,5	3569,5	2309,5	2188,5	3198,5	2047,5
hsa_miR_135a	1642,5	1711	3042,5	2762	2114	2625	1511,5	1834,5	1631,5	1989
hsa_miR_186	1995,5	1393	2996,5	2149,5	1759,5	1518	1461,5	1706,5	1918,5	1934,5
hsa_miR_192	2045,5	1495	2842	2185	1549,5	1650,5	1309,5	1515,5	1745,5	1781,5
hsa_miR_375	2159,5	1677	2525	3057	1585	1692,5	1295,5	1379	1806	2234
hsa_miR_217	2218	1636	2505	2485,5	2137,5	2117	1727,5	1669	2442,5	1758
hsa_miR_30a_3p	1393,5	1829,5	3095	3008,5	2354	3343	1772	2271,5	2093	2694,5
hsa_miR_524	2178	1349	2789,5	1971	1618,5	1314,5	1316	1488,5	1450,5	1681,5
hsa_miR_500	1879,5	1705	2716,5	2612,5	2063	2170	1656,5	1748	1715,5	2561
hsa_miR_190	1520	1767,5	3003	2331,5	2001,5	1949	1501	1914	1498	1981
hsa_miR_512_5p	1687,5	1318	3281	2420,5	2269,5	1974,5	1717	1821	1453	1695
hsa_miR_455	2242	1579	2423,5	2855	1604,5	1761	1378,5	1322	1784	2270,5
hsa_miR_34c	1606,5	1553,5	3069	2449	2127,5	2397,5	1571,5	1799,5	1885	1949,5
hsa_miR_431	2213,5	1646	2362,5	2947	1675	1464,5	1322,5	1332,5	4077,5	2030,5

hsa_miR_301	1763	1479,5	2961,5	2230,5	1861,5	2011	1299	1751	1862	1843,5
hsa_miR_28	1535,5	1699	2969	3461	2461	3051	2053,5	1923	3222	1907
hsa_miR_27b	1507,5	1404	3287	2411,5	2308,5	2501	2652,5	2140	3292,5	2158
hsa_miR_34b	1624,5	1485,5	3085,5	2280	1914,5	2078	1668	1682,5	2340,5	1833,5
hsa_miR_376a_AS	2499,5	1486,5	2188	2239	1693,5	1308	1364	1331	1831,5	1628
hsa_miR_151	1845	1587	2735,5	2585	2100,5	1979,5	1689,5	1677,5	1987,5	1720
hsa_miR_18a_AS	2289	1378,5	2485,5	2073	1311,5	1234	1116,5	1283,5	1416,5	1600
hsa_miR_323	1662,5	1607,5	2881	2928	2061	2602	1568,5	1732,5	1688	2473,5
hsa_miR_326	1965	1310	2875,5	2193	1732	1704	1271,5	1798,5	1648,5	1930,5
hsa_miR_20a	1627,5	1517,5	2975,5	2789	2731	3086	1885	1711	3055	1870,5
hsa_miR_452	1685	1546,5	2862	2269	1893	1980,5	1338,5	1486	1742	1824
hsa_miR_520h	2140,5	1312,5	2617	2248,5	1662,5	1512,5	1351,5	1773	1901,5	1927
hsa_miR_493_5p	1677,5	1662,5	2720	2592	1841	2770	1810	1477,5	1681,5	2708,5
hsa_miR_544	1701	1546	2807,5	2499	1828,5	1934,5	1520,5	1529	1529	1925,5
hsa_miR_520a_AS	2117	1535,5	2377,5	2212,5	2003,5	1411,5	1298,5	1747,5	1767,5	1845,5
hsa_miR_302a_AS	1636	1419,5	2970,5	2190,5	1895	1963,5	1292,5	1792,5	1342	1769,5
hsa_miR_106b	1349,5	1457	3209	2608,5	2054	2190	1661	1688	3020,5	1984
hsa_miR_138	1933	1434	2593	3057,5	2162	1669	1447	1438	2107,5	1819,5
hsa_miR_9	1811,5	1434	2707,5	3002,5	2859,5	1891,5	1739	2147,5	2908,5	2563,5
hsa_miR_518c_AS	1413,5	1581	2946,5	2437	1988,5	1840	1486,5	3152	1512,5	2217,5
hsa_miR_369_5p	1660	1393,5	2879	2293,5	1930	1975,5	1469,5	1885	1552,5	1865,5
hsa_miR_141	1568	1574,5	2778,5	2461	1909,5	1833	1393,5	1599	1388	1771,5
hsa_miR_517b	1927	1522	2456,5	2187,5	1668	1424	1219,5	1523	2116,5	1762,5
hsa_miR_144	2127	1366,5	2394	1943,5	1959	1291	1243	3409,5	1568	1719,5
hsa_miR_31	1431,5	1470,5	2972	4248	6157	6071	4959,5	3468,5	5165,5	3780,5
hsa_miR_188	1553	1669	2650,5	2800,5	1893,5	1971,5	1400,5	1671	2680,5	2005
hsa_miR_362	1357,5	1686	2816	2742	2081	2007,5	1505	1788,5	1962,5	2005,5
hsa_miR_299_3p	1816	1500	2532,5	2145	1459,5	1328,5	1191	1377,5	1556,5	1638,5
hsa_miR_200a_AS	1700	1528	2610,5	2231	1714,5	1598	1343,5	1508	1525,5	1883,5
hsa_miR_224	1440,5	1448	2942,5	2372	2206	2195,5	1773,5	1714	1850	1748,5
hsa_miR_142_3p	1394,5	1777,5	2657,5	2795	1840	3026,5	1498,5	1647,5	1571	2048,5
hsa_miR_148a	1659	1427,5	2736	1949	1450,5	1237	1212,5	1327	1951,5	1726
hsa_miR_143	1453,5	1612,5	2753,5	3153	1941,5	2355,5	1570	1851	2066	1997
hsa_miR_325	1797	1529	2481,5	2398	1665	1576	1341	1422,5	2246	1941
hsa_miR_193a	1874,5	1490,5	2426,5	2064,5	1458	1319	1132	1376	1541	1718
hsa_miR_492	1791	1465	2531,5	1989,5	1367	1356,5	1153	1398,5	1458,5	1610,5

hsa_miR_196a	1624	1552	2609	2341	2174,5	2081,5	1684	2124,5	1663,5	1813,5
hsa_miR_206	1362,5	1771	2636	2724	1884,5	2810,5	1405	1610	1683	2021
hsa_miR_202	1886	1350	2518,5	2493,5	1655,5	1732,5	1322	1370,5	1723,5	1678
hsa_miR_494	1735,5	1305	2713,5	2461	2210,5	2164	1776	2153	2041,5	2231
hsa_miR_485_3p	1874	1412,5	2467	2174	1741,5	1454	1358,5	1326,5	2340,5	1685,5
hsa_miR_515_5p	1911,5	1465,5	2366,5	2712	1523,5	2130	1506,5	1451,5	1629	2137,5
hsa_miR_542_3p	2330	954	2457,5	2531,5	1911	1860,5	1264	1537,5	1317,5	1754
hsa_miR_429	1506,5	1394,5	2835	2272	1618,5	1598,5	1243,5	1610,5	1700,5	1796
hsa_miR_101	2014	1486,5	2233	2329	1514	1457,5	1308,5	1241,5	2269	1970
hsa_miR_136	2029	1335,5	2346,5	2589	3467	2983	3177,5	2390	3376,5	1802
hsa_miR_205	1800	1443,5	2458,5	2414,5	1722,5	1591	1309	1505,5	1489,5	1728,5
hsa_miR_152	1721	1461	2518	2207	1886	1756,5	1575,5	1554,5	1793	1729,5
hsa_miR_18a	1958,5	1341,5	2395,5	2070	1696,5	1360	1334	1515,5	1475	1729
hsa_miR_189	1451,5	1469	2768,5	2237	1654	1503,5	1282	1507,5	1451,5	1837
hsa_miR_132	1352,5	1150	3177,5	3247	1980	3008,5	1450,5	2056	1909	2419
hsa_miR_187	1528,5	1450,5	2694	2103,5	1786	1662	1349	1485,5	1465,5	1707
hsa_miR_486	1958,5	1491,5	2216,5	2414,5	1567,5	1298	1274,5	1309,5	2313,5	1993,5
hsa_miR_453	1483,5	1601	2578	3406	2127	1593	1407,5	1566	3236,5	2428,5
hsa_miR_505	1512	1442,5	2696	2168,5	1682,5	1612	1370,5	1478	2405,5	1758,5
hsa_miR_302c	1856,5	1469,5	2322	2093	1755	1351,5	1349,5	1433,5	1285	1996,5
hsa_miR_216	1455,5	1433	2758,5	3079,5	2386	2812,5	1820	2270	1863,5	2077
hsa_miR_487b	1904,5	1281,5	2460	2339	1918,5	1421,5	1500,5	1753	1513	1976
hsa_miR_518a	1350,5	1484,5	2807	2279	1955,5	2031	1492	2334,5	2164	1956,5
hsa_miR_488	1444	1376	2811	2284	1622	1701,5	1252	1609,5	1745	1720
hsa_miR_181d	1448	1437	2741,5	2304,5	2498	2263	2188	1660,5	1887	1903,5
hsa_miR_213	1261,5	1693	2666	2550	2059,5	2732	1600,5	1621,5	1834	2398
hsa_miR_520c	1886	1327,5	2399	2125	1703	1236,5	1309,5	1563,5	1369	1722,5
hsa_miR_208	1509	1261	2842	2506	1949	1609	1533	1798	1822,5	1834,5
hsa_miR_193b	1814,5	1523	2272	2135	1555,5	1309	1313,5	1407,5	1404,5	1763
hsa_miR_337	1970	1487,5	2149,5	2508,5	1570,5	2382	1634,5	1276	1726	2679
hsa_miR_346	1355,5	1304,5	2947	1944	1524	1368,5	1206	1459	1599	1674,5
hsa_miR_125b	1589	1565	2447	3458	2700,5	4396	3630,5	1930,5	4152	3162,5
hsa_miR_128b	1935	1448	2217	2483	1562,5	1556	1561	1318	1628	2243,5
hsa_miR_339	1523	1319	2749,5	2368	1621	1458	1336	1629,5	1609,5	1775
hsa_miR_517_AS	1520,5	1550	2506,5	3032	1644,5	1586	1364,5	1402,5	2070,5	2159
hsa_miR_539	2278,5	1141,5	2154,5	2542	1809	1347,5	1443	1377	1053,5	1542

hsa_miR_92	1454,5	1497	2615	2404	1951,5	1732	1656,5	1371,5	3026	1837
hsa_miR_449	1590,5	1468,5	2498,5	2254,5	1777,5	1671	1353,5	1403,5	1412,5	1908
hsa_miR_520d_AS	1793,5	1465	2289,5	2585	1535	1413	1326	1189	2208,5	1924,5
hsa_miR_542_5p	1400	1454,5	2690,5	2391,5	1867	1821,5	1466	1494,5	1353	1790,5
hsa_miR_154_AS	1706	1283	2511	2080	1740	1523,5	1282,5	1714	1844,5	1784
hsa_miR_299_5p	1940,5	1442	2114	2628,5	1525,5	1207,5	1285,5	1214	2083	2163,5
hsa_miR_526c	1823,5	1239,5	2430	2070,5	1498	1195,5	1122,5	1394	1225	1600
hsa_miR_181c	1229	1719,5	2543	2900	1820,5	2030,5	1551,5	1720	1793,5	2208
hsa_miR_506	1877,5	1323,5	2273,5	1874	1527	1087,5	1205,5	1518	1272	1630
hsa_miR_200b	1545	1397	2532	2075	1648	1352,5	1314	1379,5	1363,5	1673
hsa_miR_519e_AS	1700	1310,5	2461,5	1932	1628,5	1462	1217,5	1438	1092,5	1617,5
hsa_miR_517c	1727,5	1366,5	2364	2060,5	1603	1357,5	1289	1722,5	1526	1675
hsa_miR_32	1570	1638	2241,5	2004	1632,5	1459,5	1383	1424	2097,5	1944,5
hsa_miR_491	1417	1160,5	2860	2566,5	2009	3653	1630,5	1965	2994	2325,5
hsa_miR_18b	1567,5	1438,5	2421	2119,5	1755,5	1549,5	1334	1355	2120	1839
hsa_miR_19a	1181,5	1557	2687,5	2590	1560	4023,5	2050,5	1885,5	1963,5	1965,5
hsa_miR_363_AS	1730	1165,5	2509	2530,5	1844	1593	1627,5	1551	1285,5	1855,5
hsa_miR_154	1471	1557,5	2321,5	2391,5	1751,5	1485,5	1464	1470,5	1521,5	1992
hsa_miR_142_5p	1173,5	1514,5	2657,5	2114,5	1503,5	1588,5	1295,5	1351,5	1457,5	1768,5
hsa_miR_214	1486,5	1553	2306	2448	1771,5	1684	1315,5	1479	1179	2237,5
hsa_miR_518b	1563,5	1217	2558,5	2110	1629	1394	1165,5	1508	1638	1691,5
hsa_miR_452_AS	1455,5	1302,5	2579	1971	1526	1483,5	1228,5	1399	1139	1609,5
hsa_miR_200a	1599,5	1283,5	2448,5	1859	1588,5	1232,5	1383,5	1440,5	1585	1643
hsa_miR_196b	1612,5	1323	2393,5	2014	1716,5	1375	1231,5	1615	1411	1851
hsa_miR_126_AS	1307	1172,5	2848	4180	4556,5	6534,5	4839,5	4150	6145,5	3175,5
hsa_miR_128a	1281	1570,5	2469,5	2293	1697	2567,5	1729	1459,5	1507,5	1922
hsa_miR_495	1529,5	1397,5	2384	2163,5	2012,5	1729	1650	1549	1758,5	1812,5
hsa_miR_516_5p	1508,5	1457	2341,5	2179	1764	1663	1295	1370	1700,5	1723,5
hsa_miR_302b_AS	1666,5	1264	2352,5	2009,5	1611,5	1328	1153	1534,5	1443,5	1665
hsa_miR_518c	1486	1296,5	2496	2023	1674	1325	1210,5	1601,5	1283	1650,5
hsa_miR_372	1390,5	1568,5	2319	2497	1814,5	1725,5	1394	1681,5	1699	2170,5
hsa_miR_489	1650	1312,5	2303	1825	1585,5	1415	1212,5	1315,5	1466,5	1632
hsa_miR_340	1418,5	1295,5	2536,5	2170	1669	1323	1207	1504,5	1570	1739
hsa_miR_302b	1398,5	1348,5	2499	2627,5	1585	1397,5	1243,5	1414	1589	1729,5
hsa_miR_126	1707,5	1288,5	2247,5	28776,5	43293,5	61388,5	43296	40640	57644,5	10800
hsa_miR_424	1350,5	1353	2533,5	2163	1121,5	774,5	926,5	904,5	1903	1316

hsa_miR_527	1326,5	1401,5	2501,5	2132,5	1757	1444	1231	1445	1644	1771
hsa_miR_100	1237,5	1128,5	2862,5	5326,5	10772,5	11400	9676,5	5156	9495,5	3478
hsa_miR_330	1369,5	1392,5	2461,5	2002,5	2020	1532	1245,5	1451,5	1268	1686,5
hsa_miR_182	1489,5	1481,5	2250	2922,5	1630,5	1561	1315	1387,5	1203	1785,5
hsa_miR_367	1867	1269,5	2084	2582	1531,5	1144	1275,5	1229	1143,5	1632
hsa_miR_508	1514,5	1368	2336	1915	1690,5	1514	1313,5	1453	1399,5	2063,5
hsa_miR_95	1182,5	1609,5	2407	2428,5	1798,5	3642,5	1497	1513,5	2501	2710
hsa_miR_517a	1397	1381,5	2411	1933	1038,5	758,5	901,5	837	837,5	1213,5
hsa_miR_493_3p	1683,5	1070,5	2434	2603	1928,5	1638,5	1523	1993	1400	1739,5
hsa_miR_509	1714,5	1409,5	2047,5	2460,5	1481,5	1524	1317	1481,5	1978	2146
hsa_miR_518a_2_A	1449,5	1473,5	2248,5	2282,5	1621	1515	1292,5	1296	1302	1715
hsa_miR_498	1536	1372,5	2258	1937,5	1649	1392,5	1366,5	1360	1346,5	2286,5
hsa_miR_133b	1453	1313,5	2392	2103	1631,5	1334,5	1253	1458,5	1296	1921,5
hsa_miR_519c	1584	1460	2113,5	2212	1623	1361,5	1254,5	1400	1158,5	2211,5
hsa_miR_302c_AS	1267	1512	2375,5	3780	1772	1798,5	1523	1391	1955,5	1795
hsa_miR_212	1442,5	1514,5	2191,5	2034	1491	1117,5	1213,5	1285	2101,5	2142,5
hsa_miR_526b	1400	1312,5	2431	2092	1701	1311,5	1317,5	1458	1461,5	1678,5
hsa_miR_382	1191	1508	2443	2411	2054	1880,5	1592,5	2651	2144,5	2579,5
hsa_miR_496	1269	1469,5	2397,5	2160	1823,5	1700	1369	1506,5	1508,5	1736
hsa_miR_211	1339	1503	2281	2845	1556,5	1488,5	1311	1662	1269,5	2062,5
hsa_miR_380_3p	1224	1419,5	2477	2168,5	1795,5	1591	1376	3029,5	1721	2081
hsa_miR_545	1195,5	1381	2529	2374	1764,5	1597,5	1398	1383	1477,5	1765
hsa_miR_518f_AS	1352	1269	2480	2085	1483	1256,5	1184	1464,5	1586,5	1661
hsa_miR_329	1502	1260,5	2332	2126	1453	1198,5	1221,5	1398,5	1373,5	1603
hsa_miR_450	1308	1405,5	2378,5	3136,5	1897	1476	1495,5	1666,5	1349	1839
hsa_miR_1	1239,5	1167,5	2670,5	2688	1918	2166	1518	1694,5	1553	2306,5
hsa_miR_497	1432	1409	2229,5	2154,5	1522,5	1328,5	1249,5	1305,5	1532	1672
hsa_miR_502	1556	1358	2151	1881	1448	1183	1187	1300,5	1409	1717,5
hsa_miR_507	1385,5	1340	2331	1998	1527	1209	1218,5	1318,5	1277	1673
hsa_miR_376b	1429,5	1250	2371,5	2204	1664	1503,5	1306	1485,5	1361	1609
hsa_miR_522	1298,5	1515	2223,5	2447	1534,5	1290,5	1263,5	1325	1234	1967
hsa_miR_99b	1258	1254,5	2517,5	2132	1650	1173	1655	1349,5	1576	1456,5
hsa_miR_137	1382,5	1333	2289	2066	1859	1729,5	1667	1691	2125,5	1886
hsa_miR_504	1112	1492,5	2400	2424	1780	2088,5	1374	1728	1305,5	1903
hsa_miR_519a	1187,5	1427,5	2386,5	2227,5	1764,5	1381	1391,5	1599	1480	1974,5
hsa_miR_218	1225,5	1505	2267	3207,5	1792	1534	1596	1603,5	2293,5	1882,5

hsa_miR_519e	1324,5	1344	2318	1955,5	1610,5	1227	1252,5	1408,5	1333	1705,5
hsa_miR_371	1427,5	1267	2283,5	1928	1563,5	1177	1213	1294	2094,5	1631,5
hsa_miR_451	1569	1222,5	2186,5	1917,5	1024	752,5	1017,5	852,5	1001,5	1366
hsa_miR_368	1334,5	1393,5	2248	2795,5	2259,5	2533	2401	2203	3078	1974,5
hsa_miR_519d	1408,5	1454	2107	2278	1515	2014	1547,5	1264	1399	2998
hsa_miR_503	1133	1535,5	2296	2276,5	1891,5	1730,5	1531,5	1535	1240	2277
hsa_miR_521	1558,5	1209	2184	1853,5	1449,5	1141	1131,5	1346	1353	1511,5
hsa_miR_130b	1344,5	1219	2377	2200	2074,5	1794	1610	1419	863,5	1619
hsa_miR_149	1558,5	1287	2083,5	1764	1527	1143,5	1189	1253	1242	1935,5
hsa_miR_210	1244,5	1280	2396,5	1749,5	1471,5	1372,5	1256	1311,5	2183,5	1618,5
hsa_miR_412	1330,5	1334	2254,5	1929	1046,5	770,5	924,5	881	884,5	1219,5
hsa_miR_520g	1254	1492	2168	2150	1628,5	1306	1263	1343	1164,5	2032
hsa_miR_409_5p	1112,5	1425	2375,5	2525	1937,5	2258	1483,5	2105	1437,5	1990,5
hsa_miR_204	1299	1331,5	2267	2051	1633	1206	1397,5	1479	1330,5	1644,5
hsa_miR_200c	1224	1489	2181,5	2170	1562	2894	1495,5	1504	1381,5	1836,5
hsa_miR_433	1290	1277,5	2321,5	1941,5	1610,5	1242,5	1180,5	1364	1280	1663,5
hsa_miR_377	1403	1285,5	2195,5	2155	1063	745,5	946,5	843,5	1448	1350
hsa_miR_514	1377	1375	2129	2030,5	1523,5	1192,5	1180,5	1327	3477	1707
hsa_miR_10b	1351	1361,5	2161	2825,5	2890	3493,5	2436	1992,5	3251	1977,5
hsa_miR_10a	1370,5	1283	2217	2266,5	2456,5	2370	2273,5	2156,5	2986	2239,5
hsa_miR_219	1297	1371,5	2199,5	2799	1705,5	2087,5	1338	1721	1327,5	1657,5
hsa_miR_524_AS	1366,5	1244	2255	2092,5	1499,5	1157	1250	1334	1311,5	1666
hsa_miR_520a	1193	1487	2178,5	2114,5	1470,5	1954	1226,5	1685,5	1768	2175,5
hsa_miR_302a	1152,5	1336	2369,5	2419,5	1777,5	1430,5	1537	1869	1525	2129
hsa_miR_134	1357,5	1444,5	2048,5	2571,5	1764	1599,5	1457	1416,5	1989,5	1893
hsa_miR_215	1234,5	1321	2269	2125	1657,5	2058	1247	2101	1552,5	1747,5
hsa_miR_127	1155,5	1495,5	2164,5	2580	1625	3024	1435	1438,5	1480	1844
hsa_miR_432_AS	1241,5	1356,5	2217,5	2410	1639,5	1500	1226,5	1331,5	1273,5	1593,5
hsa_miR_345	1368	1237,5	2202,5	2117	1509	1141,5	1254,5	1243,5	1385	1508,5
hsa_miR_520f	1254,5	1263	2260,5	2329,5	1094	1445	970	979,5	786	1361
hsa_miR_523	1308,5	1229	2237	2162,5	1418	1159	1117,5	1358,5	1302	1637,5
hsa_miR_379	1347	1283	2139,5	1881,5	1671	1325,5	1471,5	1388	1576,5	1683,5
hsa_miR_369_3p	1217	1409,5	2142	2442	1630	1400	1370	1818	1343	1746,5
hsa_miR_199b	1173,5	1422,5	2172	2264,5	1511,5	1269,5	1267,5	1193,5	1389	1709,5
hsa_miR_199a_AS	1348,5	1341	2078	2325,5	1820,5	2046	1360	1274,5	1417	1709,5
hsa_miR_376a	1459	1254,5	2043	1990,5	1754,5	1916,5	1680	1512	2510	1882

hsa_miR_199a	1131,5	1330,5	2286,5	2103	1753,5	1415	1312,5	3110	1326,5	1988,5
hsa_miR_409_3p	1125,5	1175	2441,5	2522,5	2101	2976	1880	2182	1739,5	2251
hsa_miR_410	1314,5	1327	2095	1975,5	1608	1353,5	1266,5	1335	1226	1629,5
hsa_miR_518d	1326,5	1373,5	2015	3707,5	1473	1168	1210	1183	2483	1700
hsa_miR_331	1096	1431	2186,5	2245,5	1746	2079	1470,5	2103,5	1399,5	1934
hsa_miR_525	1246	1373,5	2090	2788,5	1543	1246,5	1231	1341,5	1318	2077
hsa_miR_139	1326	1246	2135	1797	1488,5	1157,5	1260,5	1246,5	1569	1545
hsa_miR_191_AS	1034,5	1393	2277,5	2310	2045	2097,5	1448,5	2073	1203,5	2267,5
hsa_miR_302d	1206,5	1306	2169,5	2230	1672,5	1239,5	1304	2042,5	1550	1944,5
hsa_miR_490	1448,5	1284	1935,5	3570	1501	1146	1244,5	1207	1151,5	1746,5
hsa_miR_512_3p	1096,5	1449	2115	2629,5	2053	3232,5	1353	1605	2490,5	3040
hsa_miR_520d	1077,5	1435	2134,5	2082,5	1662	2191	1490	1609,5	1521	2038,5
hsa_miR_197	1285	1430,5	1926,5	3164,5	1441	987	1228,5	1245	1075,5	1943,5
hsa_miR_133a	1193,5	1360,5	2086,5	2211,5	1531	1676,5	1220	1235	1275,5	1713
hsa_miR_526a	1334,5	1284,5	2003,5	2126	1491,5	1148	1202,5	1230	1789,5	1675,5
hsa_miR_105	1076,5	1411,5	2128,5	2733	1663,5	1337,5	1275	1626	1296	1885
hsa_miR_520e	1045	1407,5	2147	2108,5	1658,5	1814,5	1353,5	1565	1638,5	2110,5
hsa_miR_487a	1070	1168,5	2347,5	2422,5	1835	1846	1769	1636	1509,5	2214
hsa_miR_363	1048,5	1426	2083,5	2526	1948,5	3052,5	1319,5	1987	1324	2773
hsa_miR_9_AS	1013	1391	2061	2050,5	1490,5	2628	1250,5	1632	1797,5	1978
hsa_miR_203	1008,5	1377	2074	2101,5	1800	3492	1342,5	2102,5	1221	2874
hsa_miR_17_3p	1248	1202	1955,5	1825,5	1518	1135,5	1285,5	1738	1138,5	1503
hsa_miR_518f	1068,5	1166,5	2164,5	2198	1662	1365,5	1331	1561,5	1369	1884
hsa_miR_365	1028,5	1263,5	2099	2014	1695	1683	1373,5	2163	1280,5	2025,5
hsa_miR_324_3p	1076,5	1175	2079,5	2179	1588	1256	1330	1447,5	1630	1803,5
hsa_miR_220	1025	1275,5	2026	1969	1542,5	1721,5	1282	1454,5	1378,5	1922,5
hsa_miR_520b	1008	1241	1985,5	1761	1443,5	1105	1250,5	1115,5	1588,5	1508,5
hsa_miR_516_3p	1416	1220	1581,5	1650,5	1567,5	1098	1266,5	1275,5	1494,5	1862,5

	normalized data										mean values		
	APC1	APC2	APC3	HUVEC1	HUVEC2	HUVEC3	HCEAC1	HCEAC2	HCEAC3	HCEAC4	APC	HUVEC	HCAEC
hsa_miR_21	12740,6	20851,2	25421,0	19486,7	16777,5	22999,8	38807,4	18340,3	22578,1	18242,6	19671,0	19754,7	30158,3
hsa_miR_223	6424,6	13188,4	15402,2	3535,1	867,3	790,9	832,4	1028,9	763,8	1144,9	11671,8	1731,1	1691
hsa_miR_16	5187,6	12574,0	15714,3	6678,0	9848,0	5599,8	8583,8	4408,3	5573,1	2356,0	11158,6	7375,3	7088,75
hsa_let_7d	3003,1	7062,3	8566,1	6852,1	12770,1	10621,6	13601,3	16937,8	28200,6	15453,4	6210,5	10081,2	25062,8
hsa_let_7f	2124,6	6129,5	9240,8	6671,0	13304,8	9349,9	9745,5	14255,9	17375,4	8736,1	5831,6	9775,2	16912,8

hsa_miR_23a	2519,1	4953,0	9354,8	5248,9	5985,8	6110,6	15900,2	6489,6	5351,3	2728,3	5609,0	5781,8	9567,25
hsa_let_7c	2404,6	4142,4	9275,2	4004,9	7103,0	9257,3	17501,7	11645,4	11972,5	28144,0	5274,1	6788,4	20288,4
hsa_let_7g	2412,1	3930,1	5877,1	4382,8	4116,9	3377,2	3358,4	3601,7	4377,9	2671,2	4073,1	3959,0	5040,63
hsa_miR_23b	1693,1	1959,8	6695,5	2527,4	6489,9	3660,1	11124,2	5538,7	6266,1	1716,5	3449,5	4225,8	8229,5
hsa_let_7b	1463,1	3139,1	5728,4	3334,3	8473,9	5244,8	8903,5	11095,7	14839,3	18440,8	3443,5	5684,3	16923,3
hsa_miR_27a	2043,6	3903,6	4191,9	5552,2	4114,0	4035,4	3325,3	5241,2	3315,3	4492,8	3379,7	4567,2	5441,88
hsa_miR_191	1766,6	2430,4	4803,9	2150,8	2689,7	1977,2	2937,9	3115,1	4399,5	3798,3	3000,3	2272,6	5065,25
hsa_let_7i	2881,6	3662,7	3285,3	3938,9	4535,4	4779,0	3362,2	3607,0	3622,2	2367,3	3276,6	4417,8	4635,25
hsa_miR_146a	2143,1	2023,3	4262,1	1678,0	1639,4	1553,9	1885,1	1581,6	1720,0	1157,8	2809,5	1623,8	2550,63
hsa_miR_103	1699,6	2747,4	4133,1	2109,1	2850,8	1708,8	3053,1	2273,8	2493,4	1718,1	2860,0	2222,9	3524,88
hsa_miR_26b	1593,1	2839,5	3955,6	2324,8	2349,6	1915,7	2167,9	1938,1	1821,4	1095,9	2796,1	2196,7	2755,5
hsa_miR_15a	1483,6	1802,7	3841,0	1467,0	1106,3	1050,9	1386,3	1218,5	1240,9	1068,9	2375,8	1208,1	2084
hsa_miR_485_5p	2220,6	2704,1	2762,0	3388,3	3109,8	2956,8	2342,6	2446,0	2153,8	2201,4	2562,2	3151,7	3348,88
hsa_miR_24	1082,1	1445,2	3921,8	2206,6	3129,8	2490,8	6951,6	2358,1	3686,3	1228,4	2149,7	2609,1	4982,63
hsa_miR_122a	1852,1	2734,8	2830,2	2527,0	2481,3	2431,0	1562,5	2390,5	1982,1	2272,5	2472,4	2479,8	3070
hsa_miR_29a	1429,1	1982,8	3102,6	4962,4	5731,3	3323,7	7502,2	5264,7	6190,8	2226,2	2171,5	4672,5	7293,88
hsa_let_7e	1588,6	1886,5	2926,5	1953,5	3325,6	3876,9	3386,2	3918,2	7192,1	7952,2	2133,9	3052,0	7618,5
hsa_miR_34a	2302,6	1982,1	2231,6	1592,7	1390,6	1789,4	2132,8	1611,4	2701,2	1710,6	2172,1	1590,9	3189,75
hsa_miR_146b	1832,6	1885,1	2485,8	1488,6	857,1	1149,0	904,9	916,1	1403,3	1063,0	2067,8	1164,9	1944,63
hsa_miR_19b	1232,6	2757,1	2418,8	3231,0	2951,2	2605,8	2346,9	2420,7	1475,0	2890,5	2136,2	2929,3	3199,75
hsa_miR_296	1285,6	2841,6	2276,2	2276,5	1703,5	2077,2	1472,3	1708,6	1442,5	3587,6	2134,5	2019,1	2918,75
hsa_miR_150	1844,6	2119,0	2139,6	1876,2	824,1	1032,0	898,1	854,9	1391,6	891,1	2034,4	1244,1	1880,5
hsa_miR_155	1399,6	2175,5	2225,4	2543,3	3676,4	2808,6	3843,3	2812,7	3311,1	2927,1	1933,5	3009,4	4527,88
hsa_miR_519b	1347,6	1158,3	2669,1	1077,7	1304,2	1366,3	2059,4	1399,6	4099,9	1059,2	1725,0	1249,4	3584,25
hsa_miR_15b	1052,1	1820,9	2504,6	1466,6	2880,2	2211,5	2468,9	1640,7	1459,3	886,8	1792,5	2186,1	2540
hsa_miR_183	1992,6	1755,2	1977,7	1325,5	1216,9	1524,0	1215,4	1528,8	1529,1	1427,7	1908,5	1355,5	2338,75
hsa_miR_145	1576,1	2110,6	2060,9	2041,8	1960,0	1751,5	1541,4	2593,0	1352,1	1491,3	1915,9	1917,8	2659
hsa_miR_106a	907,6	1538,1	2690,9	2437,3	2761,9	2031,9	2056,5	1436,9	1979,6	1464,4	1712,2	2410,4	2741,5
hsa_miR_22	1332,6	1070,3	2585,1	1097,0	1090,8	1305,5	2582,6	1264,2	2452,3	1842,6	1662,7	1164,5	3128,63
hsa_miR_499	1379,6	1961,2	2038,5	1555,8	1563,6	1754,6	1365,7	1440,9	1517,0	1189,1	1793,1	1624,7	2292,38
hsa_miR_99a	2207,6	1389,4	1758,8	2391,2	4242,1	3189,6	5424,1	3907,1	4881,7	1952,5	1785,3	3274,3	5722,63
hsa_miR_202_AS	1455,1	1692,4	1911,9	1714,9	1769,2	1600,6	1491,0	2109,5	1363,0	1654,0	1686,5	1694,9	2552,38
hsa_miR_140	1376,1	2035,2	1748,2	2108,6	1511,4	1528,3	1407,5	1212,2	2356,5	1353,9	1719,8	1716,1	2651,88
hsa_miR_30a_5p	1427,1	1905,3	1738,2	2407,5	2664,9	2189,7	3297,0	2220,0	2546,6	1303,8	1690,2	2420,7	3500,88
hsa_miR_181b	1660,6	1648,4	1652,1	1587,9	1560,3	1554,3	2382,5	1195,8	1902,3	1637,9	1653,7	1567,5	2764,25
hsa_miR_30d	1142,1	1311,9	2077,9	1657,3	2073,0	1450,2	3374,7	1660,6	2370,0	1515,0	1510,6	1726,9	3333,75

hsa_miR_511	1817,6	1450,1	1613,0	1252,6	956,7	1277,2	1045,5	1105,3	1092,5	1075,4	1626,9	1162,2	1898,63
hsa_miR_17_5p	1770,1	1052,8	1787,0	1576,9	2186,4	1927,2	2085,3	1368,1	2658,4	1480,5	1536,7	1896,9	3036,38
hsa_miR_374	1115,1	1979,3	1768,8	2463,7	1874,0	1812,8	1648,9	1930,6	2876,5	1755,3	1621,1	2050,2	3242,25
hsa_miR_30b	1686,6	855,2	1778,2	726,6	1068,4	813,3	1291,8	1101,7	1025,6	803,9	1440,0	869,4	1868,88
hsa_miR_30e_5p	913,6	1165,2	2071,7	1906,9	294,3	494,7	514,1	244,0	484,6	325,4	1383,5	898,6	1072,38
hsa_miR_425	1794,6	1592,5	1292,1	1301,4	1242,6	1317,8	1023,9	1310,4	1095,0	1143,3	1559,8	1287,3	1967,63
hsa_miR_338	1370,6	1732,9	1460,2	1217,4	847,8	1000,4	835,2	809,6	1346,2	1145,4	1521,2	1021,8	1890,13
hsa_miR_25	990,6	1802,7	1640,4	1634,9	1023,5	2453,1	1755,0	1258,9	1366,9	1278,0	1477,9	1703,8	2296,13
hsa_miR_483	1065,6	2468,8	1315,6	784,1	762,1	790,9	767,6	898,8	633,9	893,3	1616,7	779,0	1521,13
hsa_miR_373	1132,1	1542,3	1659,2	1660,4	1677,8	1587,7	1377,7	1631,8	1153,0	1629,2	1444,5	1642,0	2288,88
hsa_miR_147	1441,1	1493,4	1471,4	999,5	997,4	1181,4	880,9	1193,2	1290,8	1224,1	1468,6	1059,4	2003,5
hsa_miR_30c	1000,1	1099,6	1888,1	1039,0	1549,7	1177,9	1927,8	1220,7	1299,7	700,4	1329,3	1255,5	2166,38
hsa_miR_130a	2102,1	1440,3	1045,3	1198,1	1225,0	1446,1	1202,0	1033,3	1421,5	1024,7	1529,3	1289,8	2054,25
hsa_miR_198	1480,1	1394,2	1400,0	1257,0	1422,0	1298,9	1124,7	1112,8	1406,4	935,3	1424,8	1326,0	2029
hsa_miR_422a	1105,1	1099,6	1700,6	1010,5	1017,8	1175,5	882,8	1236,7	1173,4	943,9	1301,8	1067,9	1898,88
hsa_miR_222	1746,1	1637,2	1078,5	3213,9	4576,2	4470,8	8972,1	3738,8	5618,4	2510,7	1487,3	4087,0	7057,5
hsa_miR_484	1723,6	1452,2	1132,0	1413,0	1041,5	1300,5	1180,4	1086,6	904,1	2343,6	1435,9	1251,7	2138,63
hsa_miR_373_AS	2063,1	1116,4	1056,2	2243,1	1828,7	1112,1	1203,9	1827,6	2740,7	2783,3	1411,9	1728,0	3275,25
hsa_miR_182_AS	1084,6	1592,5	1419,4	1979,0	1394,7	1270,8	1066,2	1238,9	1301,1	969,3	1365,5	1548,2	2010,13
hsa_miR_361	1939,1	1222,5	965,1	1128,2	916,7	834,8	1218,3	816,7	1906,8	1182,1	1375,6	959,9	2250,63
hsa_miR_513	1112,1	1191,1	1453,5	1208,2	1154,5	1257,7	1089,2	1250,0	1169,2	787,2	1252,2	1206,8	1918,13
hsa_miR_448	1063,6	1510,8	1334,5	1271,0	256,3	497,8	423,8	206,2	428,3	216,1	1303,0	675,1	987,75
hsa_miR_423	1098,1	1029,8	1506,1	914,2	1126,3	1038,2	1169,8	1275,7	1098,7	1069,5	1211,3	1026,3	1980,38
hsa_miR_29b	1695,6	1091,2	1127,3	1772,5	936,3	1601,0	1263,5	905,5	1608,9	1144,9	1304,7	1436,6	2145,75
hsa_miR_7	1212,6	1399,8	1280,4	1239,0	1409,4	1107,2	1086,8	1069,7	1086,4	1032,8	1297,6	1251,8	1886,75
hsa_miR_370	1100,1	1543,0	1274,8	2170,6	1373,5	1645,3	1213,0	1345,9	1258,6	1248,3	1306,0	1729,8	2124,25
hsa_miR_93	928,6	1311,9	1454,1	2170,6	1630,1	1602,3	1401,2	955,2	2106,7	1149,2	1231,5	1801,0	2418,88
hsa_miR_221	944,6	1409,6	1390,6	3299,5	6489,1	4732,9	8131,1	4576,1	5582,0	2017,1	1248,3	4840,5	6943,5
hsa_miR_125a	622,6	1414,5	1571,9	887,0	1207,9	1236,6	2417,0	1296,2	1335,3	1703,6	1203,0	1110,5	2563,63
hsa_miR_185	1088,6	768,0	1519,0	767,4	802,9	722,7	773,8	878,4	913,9	1024,7	1125,2	764,3	1672,5
hsa_miR_33	1080,1	1061,2	1393,5	1479,8	869,4	977,5	894,8	1233,6	1212,9	1195,0	1178,3	1108,9	1977
hsa_miR_335	1756,6	1153,4	946,3	1120,8	1495,5	841,8	841,5	1318,4	954,5	1523,6	1285,4	1152,7	1947,88
hsa_miR_195	1314,6	930,6	1270,7	2938,3	1479,1	1080,4	1334,0	1151,0	1428,3	759,7	1172,0	1832,6	2063,25
hsa_miR_98	1128,6	1077,3	1313,9	850,1	1369,4	1277,8	1134,8	1224,2	1624,8	1224,6	1173,3	1165,8	2227,63
hsa_miR_422b	838,6	1163,1	1419,1	1059,2	849,8	977,1	763,2	813,6	1676,9	729,0	1140,3	962,1	1923,5
hsa_miR_383	1084,1	1331,4	1189,6	2050,2	1270,3	1186,6	1002,8	1198,5	1074,0	1225,2	1201,7	1502,4	1940,25

hsa_miR_96	1565,6	1091,2	1006,8	2331,9	995,0	1516,2	1288,4	876,6	2238,6	3093,1	1221,2	1614,4	2877,25
hsa_miR_515_3p	970,6	1233,7	1279,8	1072,0	1043,9	1111,1	902,9	953,9	1018,0	794,7	1161,4	1075,7	1720,5
hsa_miR_526b_AS	1594,6	1124,7	925,1	901,0	723,8	915,8	753,2	826,0	941,0	908,4	1214,8	846,9	1637,5
hsa_miR_194	1423,1	1055,6	1052,9	890,5	724,2	885,4	776,2	980,1	902,7	942,3	1177,2	833,3	1677,63
hsa_miR_378	1047,6	1260,2	1175,8	974,9	884,9	1047,4	912,5	892,6	1279,3	961,7	1161,2	969,0	1861,13
hsa_miR_432	788,6	1370,5	1277,2	1449,5	1417,6	1286,4	1234,2	1731,2	1015,0	1721,4	1145,4	1384,5	2239,25
hsa_miR_153	1324,1	1040,3	1083,2	915,5	1015,0	993,3	928,9	1097,3	863,5	692,9	1149,2	974,6	1675
hsa_miR_384	1052,1	1421,5	1058,8	1351,0	1228,7	1221,2	1039,7	1659,3	904,4	1067,3	1177,5	1267,0	1967,25
hsa_miR_29c	734,6	773,5	1516,3	1117,2	1242,6	1092,7	1605,3	1209,1	2190,7	606,1	1008,2	1150,8	2455
hsa_miR_342	705,1	825,9	1494,9	1117,7	867,3	952,3	1082,5	862,0	1055,6	768,3	1008,6	979,1	1752
hsa_miR_501	1158,6	1271,4	1018,3	978,4	951,8	1030,2	902,9	926,8	1307,9	879,8	1149,4	986,8	1862
hsa_miR_525_AS	1602,1	643,7	1008,9	1162,5	1341,7	1040,0	1377,7	1253,1	1486,8	652,5	1084,9	1181,4	2104,63
hsa_miR_135b	928,1	929,9	1281,3	953,8	836,3	980,6	802,6	1032,9	624,6	925,6	1046,5	923,6	1571,38
hsa_miR_20b	1020,6	767,3	1284,2	1233,3	2140,7	1562,1	1722,4	1408,5	1702,1	1091,0	1024,0	1645,4	2436
hsa_miR_135a	950,1	1229,5	1099,1	1266,7	1110,0	1193,3	956,2	1094,2	824,5	1028,0	1092,9	1190,0	1741,63
hsa_miR_186	1303,1	785,4	1072,0	728,3	820,8	761,0	908,2	980,5	985,3	969,3	1053,5	770,0	1755,25
hsa_miR_192	1353,1	927,8	981,2	759,5	649,5	812,7	762,3	810,9	888,4	804,4	1087,4	740,6	1588
hsa_miR_375	1467,1	1182,0	794,9	1525,9	678,5	829,1	748,8	689,7	922,3	1292,0	1148,0	1011,2	1678,63
hsa_miR_217	1525,6	1124,7	783,2	1023,6	1129,2	994,9	1163,6	947,2	1278,7	779,1	1144,5	1049,2	1899,25
hsa_miR_30a_3p	701,1	1394,9	1129,9	1483,3	1305,8	1473,7	1206,3	1482,2	1083,0	1788,2	1075,3	1420,9	2207,75
hsa_miR_524	1485,6	724,0	950,4	571,4	705,8	681,5	768,5	786,9	723,2	696,6	1053,3	652,9	1484,13
hsa_miR_500	1187,1	1221,1	907,5	1135,3	1068,4	1015,6	1095,4	1017,3	871,6	1644,3	1105,2	1073,1	1920,25
hsa_miR_190	827,6	1308,4	1075,9	888,3	1018,2	929,3	946,1	1164,7	749,8	1019,4	1070,6	945,3	1723,5
hsa_miR_512_5p	995,1	680,7	1239,2	966,5	1236,9	939,2	1153,5	1082,2	724,6	711,2	971,7	1047,5	1671,5
hsa_miR_455	1549,6	1045,1	735,3	1348,4	694,4	855,9	828,5	639,1	910,0	1331,3	1110,0	966,2	1688,75
hsa_miR_34c	914,1	1009,5	1114,7	991,6	1121,0	1104,4	1013,8	1063,1	966,5	985,4	1012,8	1072,3	1801,38
hsa_miR_431	1521,1	1138,7	699,4	1429,2	751,9	740,1	774,8	648,4	2194,4	1072,7	1119,8	973,7	2190,75
hsa_miR_301	1070,6	906,2	1051,5	799,5	904,0	953,5	752,2	1020,0	953,6	871,2	1009,4	885,7	1688,88
hsa_miR_28	843,1	1212,7	1055,9	1881,0	1393,1	1359,6	1476,6	1172,7	1715,3	939,6	1037,2	1544,6	2276,38
hsa_miR_27b	815,1	800,8	1242,8	958,6	1268,7	1144,9	2051,7	1365,4	1754,8	1210,1	952,9	1124,0	2560,75
hsa_miR_34b	932,1	914,6	1124,4	843,0	947,3	979,7	1106,5	959,2	1221,6	860,4	990,4	923,3	1881,13
hsa_miR_376a_AS	1807,1	916,0	596,9	807,0	767,0	679,0	814,6	647,1	936,6	639,0	1106,7	751,0	1538,63
hsa_miR_151	1152,6	1056,3	918,7	1111,1	1099,0	941,2	1127,1	954,7	1023,9	738,1	1042,5	1050,4	1768,63
hsa_miR_18a_AS	1596,6	765,2	771,7	661,1	455,4	650,1	577,0	604,9	704,1	608,8	1044,5	588,8	1354,13
hsa_miR_323	970,1	1084,9	1004,2	1412,5	1066,8	1184,3	1010,9	1003,6	856,2	1550,0	1019,8	1221,2	1865,63
hsa_miR_326	1272,6	669,5	1000,9	766,6	798,4	833,6	725,8	1062,2	834,1	964,9	981,0	799,5	1662,25

hsa_miR_20a	935,1	959,3	1059,7	1290,4	1613,3	1373,3	1314,8	984,5	1621,8	900,3	984,7	1425,7	2130,38
hsa_miR_452	992,6	999,8	993,0	833,4	929,7	941,6	790,1	784,7	886,4	850,2	995,1	901,6	1597,63
hsa_miR_520h	1448,1	673,0	849,0	815,3	741,7	758,8	802,6	1039,5	975,8	961,2	990,1	772,0	1738,25
hsa_miR_493_5p	985,1	1161,7	909,5	1117,2	887,3	1249,9	1242,8	777,2	852,5	1803,3	1018,8	1084,8	1919,38
hsa_miR_544	1008,6	999,1	961,0	1035,5	877,1	923,6	964,9	822,9	767,1	959,6	989,6	945,4	1626
hsa_miR_520a_AS	1424,6	984,4	708,3	783,7	1019,9	719,4	751,7	1016,9	900,7	873,4	1039,1	841,0	1664,75
hsa_miR_302a_AS	943,6	822,4	1056,8	764,4	931,4	935,0	746,0	1056,9	662,4	791,5	940,9	876,9	1549,13
hsa_miR_106b	657,1	874,8	1196,9	1131,7	1061,1	1023,4	1099,8	964,1	1602,4	1022,6	909,6	1072,1	2088,38
hsa_miR_138	1240,6	842,7	834,9	1526,4	1149,2	819,9	894,3	742,1	1091,1	845,3	972,7	1165,2	1703
hsa_miR_9	1119,1	842,7	902,2	1478,0	1718,2	906,8	1174,6	1372,1	1539,7	1647,0	954,7	1367,7	2339,63
hsa_miR_518c_AS	721,1	1047,9	1042,7	981,0	1007,6	886,7	932,2	2264,0	757,9	1274,2	937,2	958,5	2092,13
hsa_miR_369_5p	967,6	786,1	1003,0	854,9	959,9	939,6	915,9	1139,0	780,3	894,9	918,9	918,1	1693,13
hsa_miR_141	875,6	1038,9	943,9	1002,1	943,2	884,0	842,9	885,0	688,2	793,6	952,8	943,1	1538
hsa_miR_517b	1234,6	965,5	754,7	761,7	746,2	724,3	675,9	817,6	1096,2	783,9	985,0	744,1	1655,38
hsa_miR_144	1434,6	748,4	718,0	547,3	983,6	672,3	698,4	2492,6	789,0	737,6	967,0	734,4	1985
hsa_miR_31	739,1	893,6	1057,6	2572,7	4408,1	2539,0	4266,7	2545,0	2803,7	2958,4	896,8	3173,3	4343,5
hsa_miR_188	860,6	1170,8	868,7	1300,5	930,1	938,1	849,6	949,0	1412,0	1045,2	966,7	1056,2	1939,25
hsa_miR_362	665,1	1194,6	966,0	1249,1	1083,1	952,1	950,0	1053,3	1009,9	1045,8	941,9	1094,8	1815,38
hsa_miR_299_3p	1123,6	934,8	799,4	724,4	576,1	687,0	648,5	688,4	782,5	650,3	952,6	662,5	1440,88
hsa_miR_200a_AS	1007,6	973,9	845,2	800,0	784,1	792,2	794,9	804,2	765,2	914,3	942,3	792,1	1565,13
hsa_miR_224	748,1	862,2	1040,3	923,9	1185,1	1025,6	1207,8	987,2	946,9	768,8	883,6	1044,8	1771,5
hsa_miR_142_3p	702,1	1322,3	872,8	1295,7	886,5	1350,1	943,7	928,1	790,7	1092,1	965,8	1177,4	1691,38
hsa_miR_148a	966,6	833,6	919,0	552,1	568,8	651,2	669,1	643,5	1003,8	744,6	906,4	590,7	1554,25
hsa_miR_143	761,1	1091,9	929,2	1610,3	969,3	1088,0	1012,4	1108,8	1067,9	1036,6	927,4	1222,5	1871
hsa_miR_325	1104,6	975,3	769,4	946,7	743,7	783,6	792,5	728,3	1168,7	976,3	949,8	824,7	1737,63
hsa_miR_193a	1182,1	921,6	737,1	653,6	574,9	683,3	591,9	687,0	773,9	736,0	946,9	637,3	1441,75
hsa_miR_492	1098,6	886,0	798,8	587,7	500,6	697,9	612,0	707,0	727,7	620,1	927,8	595,4	1405,13
hsa_miR_196a	931,6	1007,4	844,3	896,6	1159,4	981,0	1121,8	1351,7	842,5	838,9	927,8	1012,3	1821,38
hsa_miR_206	670,1	1313,3	860,2	1233,3	922,8	1265,7	854,0	894,8	853,4	1062,5	947,9	1140,6	1679,75
hsa_miR_202	1193,6	725,4	791,1	1030,7	736,0	844,7	774,3	682,2	876,1	692,9	903,4	870,5	1523,5
hsa_miR_494	1043,1	662,5	905,7	1002,1	1188,7	1013,3	1210,2	1377,0	1054,2	1288,7	870,5	1068,0	2050,38
hsa_miR_485_3p	1181,6	812,6	760,9	749,9	806,1	736,0	809,3	643,1	1221,6	701,0	918,4	764,0	1677,75
hsa_miR_515_5p	1219,1	886,6	701,8	1222,7	628,3	1000,0	951,4	754,1	823,1	1188,0	935,9	950,3	1681,13
hsa_miR_542_3p	1637,6	172,4	755,3	1064,1	944,4	894,7	718,6	830,4	648,7	774,8	855,1	967,7	1468,25
hsa_miR_429	814,1	787,5	977,1	836,0	705,8	792,4	698,9	895,3	863,2	820,0	859,6	778,1	1587,63
hsa_miR_101	1321,6	916,0	623,3	886,1	620,6	737,4	761,3	567,6	1181,6	1007,5	953,7	748,0	1697,25

hsa_miR_136	1336,6	705,1	690,0	1114,6	2213,7	1333,1	2555,8	1587,4	1801,8	826,5	910,6	1553,8	2686,5
hsa_miR_205	1107,6	855,9	755,9	961,2	790,6	789,5	761,8	802,0	745,0	747,3	906,5	847,1	1508,13
hsa_miR_152	1028,6	880,4	790,8	778,9	924,0	854,1	1017,7	845,5	915,0	748,4	899,9	852,3	1663,13
hsa_miR_18a	1266,1	713,5	718,8	658,5	769,4	699,3	785,8	810,9	736,9	747,8	899,5	709,1	1513,38
hsa_miR_189	759,1	891,5	938,1	805,2	734,8	755,3	735,9	803,8	723,7	864,2	862,9	765,1	1519,5
hsa_miR_132	660,1	446,1	1178,4	1692,9	1000,7	1343,0	897,7	1290,8	980,0	1491,3	761,5	1345,6	1958,63
hsa_miR_187	836,1	865,7	894,3	687,9	842,5	817,2	800,2	784,3	731,6	724,1	865,4	782,5	1501,75
hsa_miR_486	1266,1	923,0	613,6	961,2	664,2	675,1	728,7	628,0	1206,5	1032,8	934,2	766,8	1722,75
hsa_miR_453	791,1	1075,9	826,1	1832,7	1120,6	790,3	856,4	855,7	1723,4	1501,6	897,7	1247,9	2159,63
hsa_miR_505	819,6	854,5	895,4	745,0	758,0	797,7	820,8	777,6	1258,0	779,6	856,5	766,9	1753,13
hsa_miR_302c	1164,1	892,2	675,6	678,7	817,2	696,0	800,7	738,1	630,5	1036,1	910,7	730,6	1516,13
hsa_miR_216	763,1	841,3	932,2	1545,7	1331,9	1266,5	1252,4	1480,8	954,5	1122,8	845,5	1381,4	2007,63
hsa_miR_487b	1212,1	629,7	756,7	894,9	950,5	723,3	945,7	1021,8	758,2	1014,0	866,2	856,2	1685,63
hsa_miR_518a	658,1	913,2	960,7	842,1	980,7	961,3	937,5	1538,1	1122,8	993,0	844,0	928,1	1986,75
hsa_miR_488	751,6	761,7	963,0	846,5	708,7	832,6	707,1	894,4	888,1	738,1	825,4	795,9	1581,63
hsa_miR_181d	755,6	846,9	922,2	864,6	1423,3	1051,9	1605,7	939,7	967,6	935,9	841,6	1113,2	1909,75
hsa_miR_213	569,1	1204,3	877,8	1080,3	1065,6	1235,1	1041,7	905,0	938,0	1468,7	883,8	1127,0	1863,5
hsa_miR_520c	1193,6	693,9	720,9	706,8	774,7	651,1	762,3	853,5	677,5	740,8	869,5	710,9	1491,13
hsa_miR_208	816,6	601,1	981,2	1041,7	975,4	796,5	976,9	1061,7	931,5	861,5	799,7	937,9	1747
hsa_miR_193b	1122,1	966,9	646,3	715,6	654,4	679,4	766,1	715,0	697,4	784,5	911,8	683,1	1472,13
hsa_miR_337	1277,6	917,4	574,3	1043,8	666,7	1098,4	1074,3	598,2	877,5	1771,5	923,1	936,3	1828,88
hsa_miR_346	663,1	661,8	1043,0	547,7	628,7	702,6	662,9	760,7	806,3	689,1	789,3	626,3	1484,63
hsa_miR_125b	896,6	1025,6	749,1	1878,4	1588,5	1884,9	2990,7	1179,4	2236,1	2292,5	890,4	1783,9	3218,88
hsa_miR_128b	1242,6	862,2	613,9	1021,4	660,1	775,8	1003,7	635,5	822,6	1302,2	906,3	819,1	1687,63
hsa_miR_339	830,6	682,1	926,9	920,4	707,9	737,6	787,7	912,1	812,2	797,4	813,2	788,6	1587,5
hsa_miR_517_AS	828,1	1004,6	784,1	1504,0	727,0	787,5	815,1	710,6	1070,4	1211,2	872,3	1006,2	1749,13
hsa_miR_539	1586,1	434,2	577,2	1073,3	861,2	694,4	890,5	687,9	500,8	546,3	865,9	876,3	1353,88
hsa_miR_92	762,1	930,6	847,8	952,0	977,5	844,6	1095,4	683,0	1605,5	864,2	846,9	924,7	1972,75
hsa_miR_449	898,1	890,8	779,4	820,6	835,5	820,7	804,5	711,5	701,9	940,7	856,1	825,6	1519,38
hsa_miR_520d_AS	1101,1	886,0	656,5	1111,1	637,7	720,0	778,1	521,0	1147,7	958,5	881,2	822,9	1662
hsa_miR_542_5p	707,6	871,3	892,2	941,0	908,5	879,5	912,5	792,3	668,6	814,1	823,7	909,7	1526
hsa_miR_154_AS	1013,6	631,8	786,7	667,2	804,9	763,1	736,4	987,2	943,8	807,1	810,7	745,1	1656,25
hsa_miR_299_5p	1248,1	853,8	553,4	1149,3	629,9	639,7	739,2	543,2	1077,4	1216,0	885,1	806,3	1686,5
hsa_miR_526c	1131,1	571,1	739,1	658,9	607,5	635,0	582,7	703,0	596,9	608,8	813,8	633,8	1335,38
hsa_miR_181c	536,6	1241,3	805,5	1387,9	870,6	961,1	994,6	992,5	915,3	1264,0	861,2	1073,2	1818,25
hsa_miR_506	1185,1	688,4	647,1	486,2	631,2	592,9	662,4	813,1	623,2	641,1	840,2	570,1	1406,38

hsa_miR_200b	852,6	791,0	799,1	662,8	729,9	696,4	766,6	690,1	674,5	687,5	814,2	696,4	1432,5
hsa_miR_519e_AS	1007,6	670,2	757,6	537,2	714,0	739,1	673,9	742,1	522,7	627,7	811,8	663,4	1341,38
hsa_miR_517c	1035,1	748,4	700,3	650,1	693,2	698,3	742,6	994,7	765,5	689,6	828,0	680,5	1553,13
hsa_miR_32	877,6	1127,5	628,3	600,4	717,2	738,1	832,8	729,7	1085,5	980,0	877,8	685,3	1712,25
hsa_miR_491	724,6	460,7	991,8	1094,8	1024,4	1594,7	1070,5	1210,0	1587,6	1390,6	725,7	1238,0	2228,75
hsa_miR_18b	875,1	848,9	733,8	702,0	817,6	773,3	785,8	668,4	1098,1	866,4	819,3	764,3	1662
hsa_miR_19a	489,1	1014,4	890,4	1115,5	658,1	1739,4	1473,7	1139,4	1010,5	1002,7	798,0	1171,0	1966,25
hsa_miR_363_AS	1037,6	467,7	785,5	1063,2	889,8	790,3	1067,6	842,4	630,8	884,1	763,6	914,4	1579,88
hsa_miR_154	778,6	1015,1	675,4	941,0	814,3	748,3	910,6	770,9	762,9	1031,2	823,0	834,5	1612
hsa_miR_142_5p	481,1	955,1	872,8	697,6	612,0	788,5	748,8	665,3	727,1	790,4	769,7	699,4	1468,25
hsa_miR_214	794,1	1008,8	666,2	990,7	830,6	825,8	768,0	778,5	571,1	1295,7	823,1	882,4	1552,75
hsa_miR_518b	871,1	539,6	814,6	693,6	714,4	712,6	624,0	804,2	828,2	707,4	741,8	706,8	1500,75
hsa_miR_452_AS	763,1	659,0	826,7	571,4	630,4	747,5	684,5	707,5	548,7	619,1	749,6	649,8	1344
hsa_miR_200a	907,1	632,5	750,0	473,0	681,3	649,5	833,3	744,3	798,5	655,2	763,2	601,3	1513
hsa_miR_196b	920,1	687,7	717,7	609,2	785,8	705,1	687,4	899,3	701,1	879,3	775,2	700,0	1527,13
hsa_miR_126_AS	614,6	477,5	984,8	2512,9	3102,5	2720,0	4151,4	3150,1	3352,5	2306,5	692,3	2778,5	4577,63
hsa_miR_128a	588,6	1033,3	762,3	854,4	769,8	1170,8	1165,0	761,2	755,1	955,8	794,7	931,7	1654,5
hsa_miR_495	837,1	791,7	712,1	740,6	1027,2	843,4	1089,2	840,7	895,7	837,8	780,3	870,4	1692,5
hsa_miR_516_5p	816,1	874,8	687,1	754,3	824,5	817,6	748,4	681,7	863,2	741,9	792,7	798,8	1522,25
hsa_miR_302b_AS	974,1	605,3	693,6	605,3	700,1	686,8	612,0	827,8	719,3	678,9	757,7	664,1	1449
hsa_miR_518c	793,6	650,7	777,9	617,1	751,1	685,6	667,2	887,3	629,4	663,2	740,7	684,6	1436,38
hsa_miR_372	698,1	1030,5	673,9	1033,7	865,7	842,0	843,4	958,3	862,3	1223,6	800,8	913,8	1736,25
hsa_miR_489	957,6	673,0	664,5	443,1	678,9	720,8	669,1	633,3	732,1	643,3	765,0	614,3	1406,63
hsa_miR_340	726,1	649,3	801,7	746,3	747,0	684,8	663,9	801,1	790,1	758,6	725,7	726,1	1505,13
hsa_miR_302b	706,1	723,3	779,7	1148,4	678,5	713,9	698,9	720,8	800,7	748,4	736,4	846,9	1494
hsa_miR_126	1015,1	639,5	631,9	24130,8	34702,5	24141,1	41073,7	35550,5	32193,6	10522,1	762,2	27658,1	38095,1
hsa_miR_424	658,1	729,6	799,9	740,2	300,4	470,6	394,6	268,4	976,6	302,8	729,2	503,7	1262,5
hsa_miR_527	634,1	797,3	781,1	713,4	818,8	732,1	686,9	748,3	831,5	793,1	737,5	754,8	1522,75
hsa_miR_100	545,1	416,1	993,3	3520,6	8173,3	4620,0	8795,5	4043,4	5228,6	2632,4	651,5	5438,0	6951,5
hsa_miR_330	677,1	784,7	757,6	599,1	1033,3	766,4	700,8	754,1	621,0	702,0	739,8	799,6	1412,88
hsa_miR_182	797,1	909,0	633,3	1407,7	715,6	777,8	767,6	697,3	584,6	808,7	779,8	967,0	1422,75
hsa_miR_367	1174,6	613,0	535,8	1108,4	634,8	614,9	729,6	556,5	551,3	643,3	774,5	786,1	1320
hsa_miR_508	822,1	750,5	683,9	522,2	764,5	759,4	766,1	755,4	694,6	1108,3	752,2	682,1	1557,38
hsa_miR_95	490,1	1087,7	725,6	973,5	852,6	1590,6	942,3	809,1	1311,5	1804,9	767,8	1138,9	2055,38
hsa_miR_517a	704,6	769,3	727,9	538,0	232,7	464,4	370,6	208,4	379,9	192,4	734,0	411,7	947,375
hsa_miR_493_3p	991,1	335,1	741,5	1126,9	958,7	808,0	967,3	1234,9	694,9	759,1	689,2	964,5	1663,88

hsa_miR_509	1022,1	808,4	514,3	1001,7	594,1	763,3	769,5	780,7	1018,6	1197,2	781,6	786,3	1730,63
hsa_miR_518a_2_A	757,1	897,8	632,4	845,2	707,9	759,8	746,0	616,0	640,0	732,7	762,5	771,0	1401,38
hsa_miR_498	843,6	756,8	638,0	542,0	730,7	712,0	817,0	672,8	664,9	1348,5	746,2	661,6	1589,88
hsa_miR_133b	760,6	674,4	716,8	687,5	716,4	689,3	708,0	760,3	636,7	955,2	717,3	697,7	1482,25
hsa_miR_519c	891,6	879,0	553,1	783,3	709,5	699,9	709,5	708,4	559,7	1267,7	774,6	730,9	1506,13
hsa_miR_302c_AS	574,6	951,6	707,1	2161,4	831,0	870,5	967,3	700,4	1006,0	818,9	744,4	1287,6	1666,13
hsa_miR_212	750,1	955,1	598,9	626,8	601,8	604,6	670,1	606,2	1087,8	1193,4	768,1	611,1	1685,63
hsa_miR_526b	707,6	673,0	739,7	677,8	773,1	680,3	770,0	759,8	729,3	693,4	706,8	710,4	1478,88
hsa_miR_382	498,6	946,0	746,8	958,2	1061,1	902,5	1034,0	1819,1	1111,8	1664,3	730,5	973,9	2241,88
hsa_miR_496	576,6	892,2	720,0	737,6	873,0	832,1	819,4	802,9	755,7	755,4	729,6	814,2	1530
hsa_miR_211	646,6	939,0	651,5	1339,6	655,2	749,5	763,7	941,0	621,8	1107,2	745,7	914,8	1576,25
hsa_miR_380_3p	531,6	822,4	766,7	745,0	850,2	789,5	826,1	2155,2	874,7	1127,1	706,9	794,9	2051,88
hsa_miR_545	503,1	768,7	797,3	925,6	824,9	792,0	847,2	693,3	738,3	786,6	689,7	847,5	1505,88
hsa_miR_518f_AS	659,6	612,3	768,5	671,6	595,3	658,9	641,8	765,6	799,3	674,6	680,1	641,9	1474
hsa_miR_329	809,6	600,4	681,5	707,7	570,8	636,2	677,8	707,0	680,1	612,1	697,2	638,2	1399,13
hsa_miR_450	615,6	802,9	708,8	1595,8	933,0	744,6	940,9	945,0	666,3	866,4	709,1	1091,1	1587,5
hsa_miR_1	547,1	470,5	880,5	1201,6	950,1	1014,0	962,5	969,8	780,6	1370,1	632,7	1055,3	1768
hsa_miR_497	739,6	807,8	621,3	732,7	627,5	687,0	704,7	624,4	768,8	686,4	722,9	682,4	1439,75
hsa_miR_502	863,6	736,5	575,1	492,3	566,7	630,2	644,7	620,0	699,9	735,4	725,1	563,1	1403,5
hsa_miR_507	693,1	711,4	680,9	595,2	631,2	640,3	674,9	636,0	626,0	687,5	695,2	622,2	1371,75
hsa_miR_376b	737,1	585,7	704,7	776,2	742,9	755,3	758,9	784,3	673,1	618,5	675,9	758,2	1440,38
hsa_miR_522	606,1	955,8	617,8	989,8	637,3	672,1	718,1	641,8	601,9	1004,3	726,6	766,4	1447,38
hsa_miR_99b	565,6	592,0	790,5	712,9	731,5	626,3	1094,0	663,5	793,5	454,2	649,4	690,2	1509,25
hsa_miR_137	690,1	701,6	656,3	654,9	902,0	843,6	1105,5	966,7	1101,2	917,0	682,7	800,2	1842,38
hsa_miR_504	419,6	924,4	721,5	969,6	837,6	983,8	824,2	999,6	642,0	935,3	688,5	930,3	1577,63
hsa_miR_519a	495,1	833,6	713,6	796,9	824,9	707,5	841,0	885,0	739,7	1012,4	680,8	776,4	1611,25
hsa_miR_218	533,1	941,8	643,3	1658,2	847,3	767,2	1037,3	889,0	1195,3	913,2	706,1	1090,9	1843,88
hsa_miR_519e	632,1	717,0	673,3	557,8	699,3	647,3	707,6	715,9	657,4	722,5	674,1	634,8	1424,88
hsa_miR_371	735,1	609,5	653,0	533,6	660,9	627,8	669,6	614,2	1083,8	642,8	665,9	607,5	1558,25
hsa_miR_451	876,6	547,3	596,0	524,4	220,8	462,0	481,9	222,2	471,7	356,7	673,3	402,4	1059,38
hsa_miR_368	642,1	786,1	632,2	1296,1	1228,7	1157,3	1810,2	1421,4	1634,6	1012,4	686,8	1227,4	2414,13
hsa_miR_519d	716,1	870,6	549,3	841,3	621,4	954,7	990,8	587,6	694,3	2115,2	712,0	805,8	1802,13
hsa_miR_503	440,6	984,4	660,4	839,9	928,5	844,0	975,4	828,2	605,3	1338,3	695,1	870,8	1645,88
hsa_miR_521	866,1	528,5	594,5	468,2	567,9	613,8	591,4	660,4	668,6	513,5	663,1	550,0	1335,5
hsa_miR_130b	652,1	542,4	708,0	772,7	1077,8	868,8	1050,8	725,2	394,4	629,3	634,2	906,4	1377,88
hsa_miR_149	866,1	637,4	535,5	389,5	631,2	614,7	646,6	577,8	606,4	970,3	679,7	545,1	1404,88

hsa_miR_210	552,1	627,6	719,4	376,8	585,9	704,2	710,9	629,8	1133,7	628,8	633,1	555,6	1592,38
hsa_miR_412	638,1	703,0	636,0	534,5	239,2	469,1	392,6	247,5	406,2	198,8	659,0	414,3	977,375
hsa_miR_520g	561,6	923,7	585,1	728,8	714,0	678,2	717,6	657,7	563,0	1074,3	690,1	707,0	1450,63
hsa_miR_409_5p	420,1	830,1	707,1	1058,4	966,0	1050,0	929,3	1334,3	715,9	1029,6	652,4	1024,8	1754,13
hsa_miR_204	606,6	699,5	643,3	641,8	717,6	639,1	846,8	778,5	656,0	656,8	649,8	666,2	1462,88
hsa_miR_200c	531,6	919,5	593,1	746,3	659,7	1298,3	940,9	800,7	684,5	863,7	681,4	901,5	1554,38
hsa_miR_433	597,6	624,1	675,4	545,5	699,3	653,4	638,4	676,4	627,7	677,2	632,4	632,7	1372
hsa_miR_377	710,6	635,3	601,3	733,2	252,7	459,3	413,8	214,2	721,8	339,4	649,1	481,7	1147
hsa_miR_514	684,6	760,3	562,2	623,7	628,3	633,9	638,4	643,5	1858,1	724,1	669,0	628,6	1922,88
hsa_miR_10b	658,6	741,4	581,0	1322,5	1743,0	1532,4	1843,8	1234,4	1731,5	1015,6	660,4	1532,6	2414,25
hsa_miR_10a	678,1	631,8	613,9	831,2	1389,4	1093,7	1687,8	1380,1	1583,1	1297,9	641,3	1104,8	2413,88
hsa_miR_219	604,6	755,4	603,7	1299,2	776,8	983,4	789,6	993,4	654,3	670,8	654,6	1019,8	1511
hsa_miR_524_AS	674,1	577,3	636,3	678,2	608,7	620,0	705,2	649,7	645,3	679,9	629,3	635,7	1390,38
hsa_miR_520a	500,6	916,7	591,3	697,6	585,1	931,2	682,6	961,9	901,0	1228,9	669,5	738,0	1713,88
hsa_miR_302a	460,1	705,8	703,6	965,6	835,5	726,8	980,7	1124,8	764,9	1178,8	623,2	842,7	1765
hsa_miR_134	665,1	857,3	514,9	1099,2	824,5	792,8	903,9	723,0	1025,0	924,5	679,1	905,5	1689
hsa_miR_215	542,1	684,9	644,5	706,8	737,6	971,9	702,3	1330,8	780,3	767,8	623,8	805,4	1662
hsa_miR_127	463,1	928,5	583,1	1106,7	711,1	1349,1	882,8	742,5	739,7	871,7	658,3	1055,6	1549,38
hsa_miR_432_AS	549,1	734,4	614,2	957,3	722,9	754,0	682,6	647,5	624,1	601,8	632,6	811,4	1356,25
hsa_miR_345	675,6	568,3	605,4	699,8	616,5	614,0	709,5	569,4	686,5	510,2	616,4	643,4	1347,88
hsa_miR_520f	562,1	603,9	639,5	886,5	277,9	732,5	436,3	335,0	351,0	351,3	601,8	632,3	1024,13
hsa_miR_523	616,1	556,4	625,7	739,7	542,3	620,8	577,9	671,5	640,0	649,2	599,4	634,3	1353,88
hsa_miR_379	654,6	631,8	568,4	492,8	748,6	685,8	917,8	697,7	793,7	698,8	618,3	642,4	1529,88
hsa_miR_369_3p	524,6	808,4	569,9	985,4	715,2	714,9	820,4	1079,5	663,0	766,7	634,3	805,2	1569,38
hsa_miR_199b	481,1	826,6	587,5	829,4	618,5	663,9	722,0	525,0	688,7	726,8	631,7	704,0	1389,88
hsa_miR_199a_AS	656,1	712,8	532,2	883,0	870,6	967,2	810,8	596,9	704,4	726,8	633,7	906,9	1440,25
hsa_miR_376a	766,6	592,0	511,7	588,6	816,8	916,6	1118,0	807,8	1316,5	912,7	623,4	774,0	1896
hsa_miR_199a	439,1	698,1	654,8	687,5	815,9	720,8	765,2	2226,7	653,7	1027,4	597,4	741,4	1934,38
hsa_miR_409_3p	433,1	481,0	745,9	1056,2	1099,4	1330,3	1310,0	1402,7	885,0	1310,3	553,3	1162,0	2013,13
hsa_miR_410	622,1	693,2	542,2	575,4	697,2	696,7	721,0	650,6	597,5	640,6	619,2	656,5	1364,25
hsa_miR_518d	634,1	758,2	495,2	2097,7	587,1	624,3	666,7	515,7	1301,4	716,6	629,2	1103,0	1644
hsa_miR_331	403,6	838,5	596,0	812,7	809,8	980,1	916,9	1333,0	694,6	968,7	612,7	867,5	1726,88
hsa_miR_525	553,6	758,2	539,3	1289,9	644,2	655,0	686,9	656,4	649,0	1122,8	617,0	863,0	1491,88
hsa_miR_139	633,6	580,1	565,7	418,5	599,8	620,2	715,2	572,1	789,5	549,6	593,2	546,2	1405,25
hsa_miR_191_AS	342,1	785,4	649,5	869,4	1053,7	987,3	895,7	1305,9	584,9	1328,1	592,3	970,1	1748,13
hsa_miR_302d	514,1	663,9	586,0	799,1	749,9	652,2	757,0	1278,8	778,9	980,0	588,0	733,7	1710,25

hsa_miR_490	756,1	633,2	448,5	1976,8	610,0	615,7	699,9	537,0	555,7	766,7	612,6	1067,5	1337,38
hsa_miR_512_3p	404,1	863,6	554,0	1150,2	1060,3	1430,5	804,0	890,4	1305,6	2160,5	607,2	1213,7	2122,13
hsa_miR_520d	385,1	844,1	565,5	669,4	741,3	1023,8	935,6	894,4	762,7	1081,3	598,2	811,5	1664,75
hsa_miR_197	592,6	837,8	443,2	1620,4	561,0	553,6	684,5	570,7	513,2	979,0	624,5	911,7	1373,13
hsa_miR_133a	501,1	740,0	537,2	782,8	634,4	822,9	676,4	561,8	625,2	730,6	592,8	746,7	1360,88
hsa_miR_526a	642,1	633,9	488,5	707,7	602,2	616,5	659,5	557,4	913,0	690,2	588,2	642,1	1474,38
hsa_miR_105	384,1	811,2	561,9	1241,2	742,5	690,5	729,2	909,0	636,7	915,9	585,8	891,4	1520,5
hsa_miR_520e	352,6	805,7	572,8	692,3	738,4	876,8	804,5	854,9	828,5	1158,9	577,0	769,2	1666,88
hsa_miR_487a	377,6	471,9	690,6	968,3	882,4	889,1	1203,4	917,9	756,2	1270,4	513,4	913,3	1782,13
hsa_miR_363	356,1	831,5	535,5	1059,2	975,0	1360,2	771,9	1229,6	652,3	1872,8	574,4	1131,5	1850,88
hsa_miR_9_AS	320,6	782,6	522,3	641,3	601,4	1194,4	705,6	914,3	917,5	1016,1	541,8	812,4	1664,5
hsa_miR_203	316,1	763,1	529,9	686,1	853,9	1531,9	794,0	1332,1	594,7	1981,6	536,4	1024,0	1885
hsa_miR_17_3p	555,6	518,7	460,3	443,6	623,8	611,6	739,2	1008,5	548,5	504,3	511,5	559,7	1416,25
hsa_miR_518f	376,1	469,1	583,1	771,0	741,3	701,4	782,9	851,8	677,5	914,8	476,1	737,9	1536,38
hsa_miR_365	336,1	604,6	544,6	609,2	768,2	825,4	823,7	1385,8	628,0	1067,3	495,1	734,3	1710,63
hsa_miR_324_3p	384,1	481,0	533,1	754,3	680,9	658,7	782,0	750,5	823,7	828,1	466,1	697,9	1552,75
hsa_miR_220	332,6	621,3	501,7	569,7	643,8	840,4	735,9	756,7	682,9	956,3	485,2	684,6	1509,38
hsa_miR_520b	315,6	573,2	477,9	386,9	563,1	599,7	705,6	455,7	800,5	510,2	455,6	516,5	1365,75
hsa_miR_516_3p	723,6	543,8	240,5	289,8	664,2	597,0	721,0	597,8	747,8	891,7	502,6	517,0	1474,75

APC= angiogenic progenitor cells

HUVEC, human umbilical vein endothelial cells

HCAECs, human coronary artery endothelial cells

Scanned data were normalized using the vsn package in R (see Supplemental Online Methods).

Row data after scanning (top; raw data) and after normalization raised to the power on the base of the natural logarithm are shown (bottom; normalized data).

Online Table II) Deregulated proteins based on a proteome approach

Protein name	accession numbers	No.on Gel	Av. Ratio	p-value
downregulated proteins by miR-21 overexpression (miR-21 precursor group / scrambled miR group)				
Superoxide dismutase [Mn]	SODM_HUMAN	1925	-1,47	0,001900
SPARC precursor	SPRC_HUMAN	989	-1,38	0,000016
Beta-2-microglobulin precursor	B2MG_HUMAN	2442	-1,37	0,000470
Heat shock cognate 71 kDa protein	HSP7C_HUMAN	459	-1,35	0,000140
BTB/POZ domain-containing protein KCTD12	KCD12_HUMAN	1328	-1,34	0,000005
Unidentified	-	2435	-1,34	0,000460
Annexin A6	ANXA6_HUMAN	458	-1,31	0,000650
Vimentin	VIME_HUMAN	2554	-1,3	0,000270
Reticulocalbin-1 precursor	RCN1_HUMAN	2554	-1,3	0,000270
Endoplasmic precursor	ENPL_HUMAN	144	-1,28	0,000024
Protein disulfide-isomerase A3 precursor	PDIA3_HUMAN	692	-1,28	0,000053
Calreticulin precursor	CALR_HUMAN	667	-1,27	0,000390
NADH-ubiquinone oxidoreductase 75 kDa subunit	NDUS1_HUMAN	336	-1,25	0,004600
Vimentin	VIME_HUMAN	592	-1,25	0,000160
Calumenin precursor	CALU_HUMAN	881	-1,25	0,001600
Protein disulfide-isomerase A3 precursor	PDIA3_HUMAN	693	-1,25	0,000200
Nuclear autoantigenic sperm protein	NASP_HUMAN	480	-1,24	0,000780
Guanine nucleotide-binding protein subunit beta-2-like 1	GBLP_HUMAN	1484	-1,24	0,003700
Actin-related protein 2/3 complex subunit 2	ARPC2_HUMAN	1484	-1,24	0,003700
Lamin-B2	LMNB2_HUMAN	466	-1,23	0,000770
Xaa-Pro dipeptidase	PEPD_HUMAN	757	-1,23	0,001700
Protein disulfide-isomerase A3 precursor	PDIA3_HUMAN	689	-1,22	0,000014
Protein disulfide-isomerase precursor	PDIA1_HUMAN	620	-1,21	0,000013
Elongation factor 2	EF2_HUMAN	224	-1,21	0,002000
Programmed cell death 6-interacting protein	PDC6I_HUMAN	224	-1,21	0,002000
Early endosome antigen 1	EEA1_HUMAN	33	-1,2	0,013000

Annexin A6	ANXA6_HUMAN	489	-1,2	0,001500
Calreticulin precursor	CALR_HUMAN	721	-1,2	0,000370
Thioredoxin domain-containing protein 5 precursor	TXND5_HUMAN	878	-1,2	0,000710
upregulated proteins by miR-21 overexpression (scrambled miR group / miR-21 precursor group)				
Cofilin-1	COF1_HUMAN	2044	1,2	0,000072
Ezrin	EZRI_HUMAN	330	1,2	0,000880
Proliferating cell nuclear antigen	PCNA_HUMAN	1371	1,22	0,000190
Proteasome subunit beta type-6 precursor	PSB6_HUMAN	1807	1,22	0,005300
Profilin-1	PROF1_HUMAN	2320	1,22	0,001500
NHP2-like protein 1	NH2L1_HUMAN	2320	1,22	0,001500
L-lactate dehydrogenase A chain	LDHA_HUMAN	1390	1,22	0,009500
Eukaryotic translation initiation factor 3 subunit J	EIF3J_HUMAN	1268	1,23	0,000920
Inorganic pyrophosphatase	IPYR_HUMAN	1403	1,24	0,000250
Proto-oncogene C-crk	CRK_HUMAN	1788	1,24	0,015000
Enoyl-CoA hydratase, mitochondrial precursor	ECHM_HUMAN	1694	1,24	0,000002
Transcription factor BTF3 homolog 4	BT3L4_HUMAN	2063	1,24	0,002200
Non-POU domain-containing octamer-binding protein	NONO_HUMAN	636	1,24	0,000780
Cathepsin D precursor	CATD_HUMAN	1563	1,25	0,000140
L-lactate dehydrogenase A chain	LDHA_HUMAN	1430	1,26	0,011000
40S ribosomal protein S3	RS3_HUMAN	1520	1,27	0,002800
Carbonyl reductase [NADPH] 1	CBR1_HUMAN	1520	1,27	0,002800
S-formylglutathione hydrolase	ESTD_HUMAN	1444	1,27	0,000025
Mitochondrial 28S ribosomal protein S6	RT06_HUMAN	2372	1,28	0,025000
Myotrophin	MTPN_HUMAN	2429	1,29	0,004800
Radixin	RADI_HUMAN	348	1,33	0,000270
Lamin-A/C	LMNA_HUMAN	348	1,33	0,000270
Unidentified	-	2441	1,37	0,000055
GTP:AMP phosphotransferase mitochondrial	KAD3_HUMAN	1723	1,39	0,002600
40S ribosomal protein S3	RS3_HUMAN	1512	1,39	0,006600
NAD(P)H dehydrogenase [quinone] 1	NQO1_HUMAN	1512	1,39	0,006600

Online Table III) Patient characteristics

	no of patients	age	sex (% male)	diabetes type II (in %)	hypertension (in %)
control	6	62.7±12.7	50.0	0	66.6
CAD, ADMA low (<0.55µM)	6	65.3±7.3	66.6	0	83.3
CAD, ADMA high (>0.55µM)	8	73.0±5.1	50.0	25	62.5