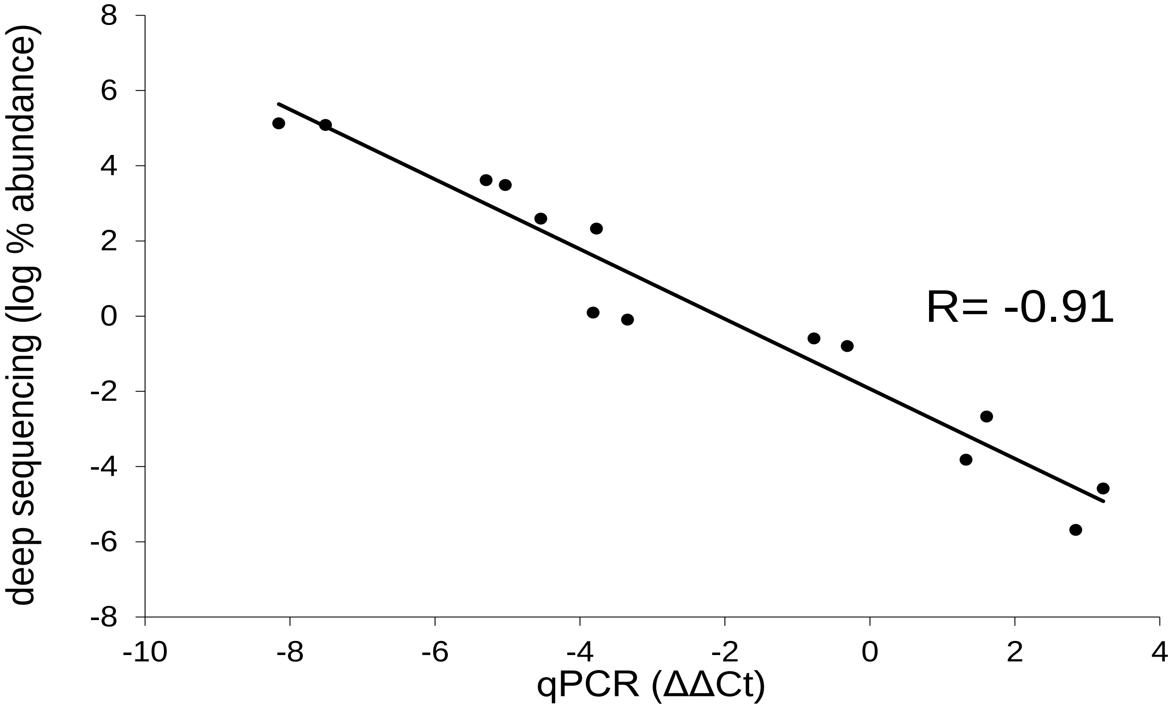
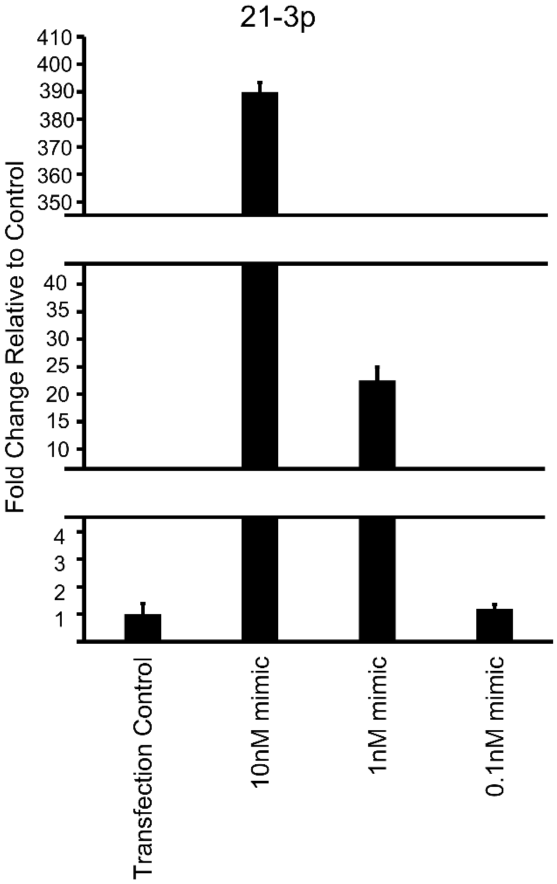
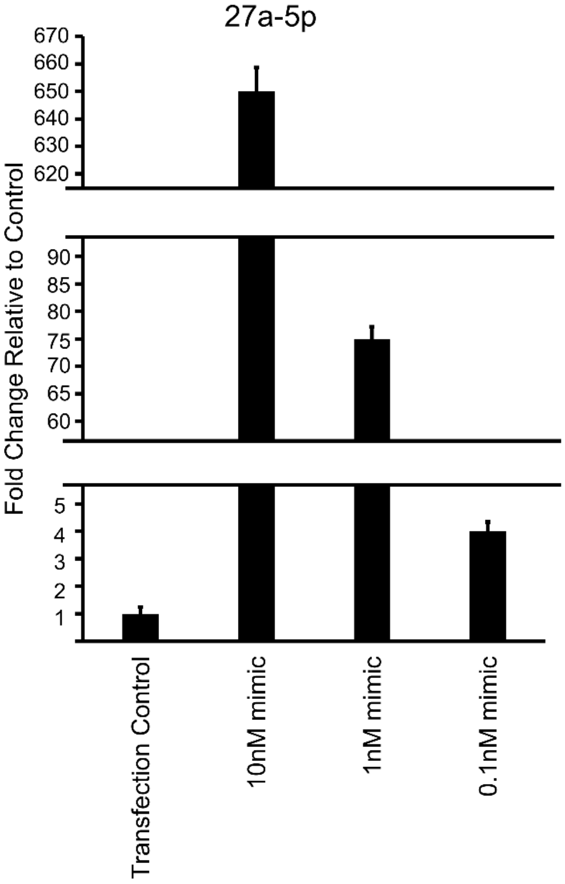
Supplementary Figures and Tables

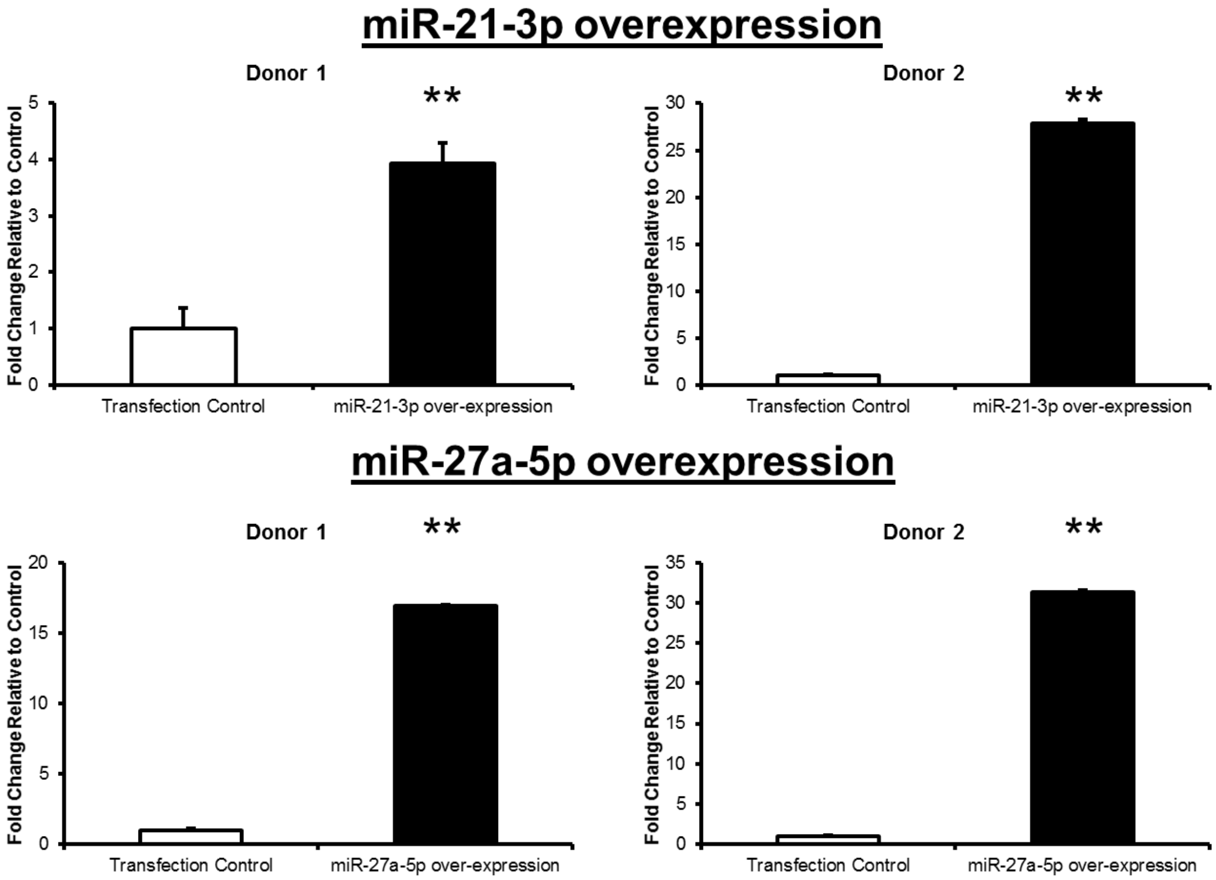


Supplementary Figure I: Pearson's correlation of miR-qPCR and deep-sequencing. miRNA-specific RT-qPCR was used to assay the expression levels of 7 miRNAs whose abundance levels varied approximately 10,000 according to deep sequencing.

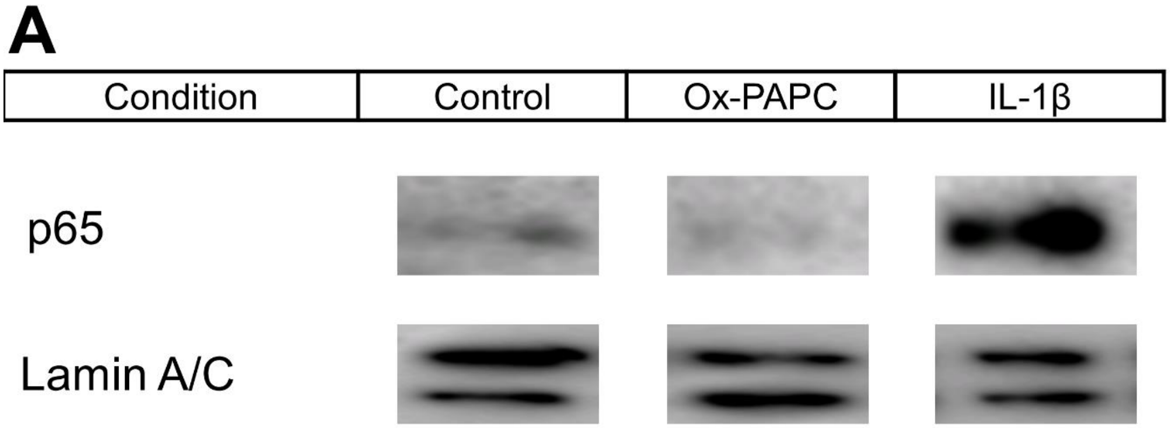




Supplementary Figure II: Dose response for over-expression of miRs-21-3p and -27a-5p in HAECs. HAECs were transfected with either 10nM, 1nM or 0.1nM miR-21-3p or -27a-5p mimic for 24 hours. miRNA expression was quantified using RT-qPCR to determine the level of over-expression. N =3, bars represent +/- SEM.



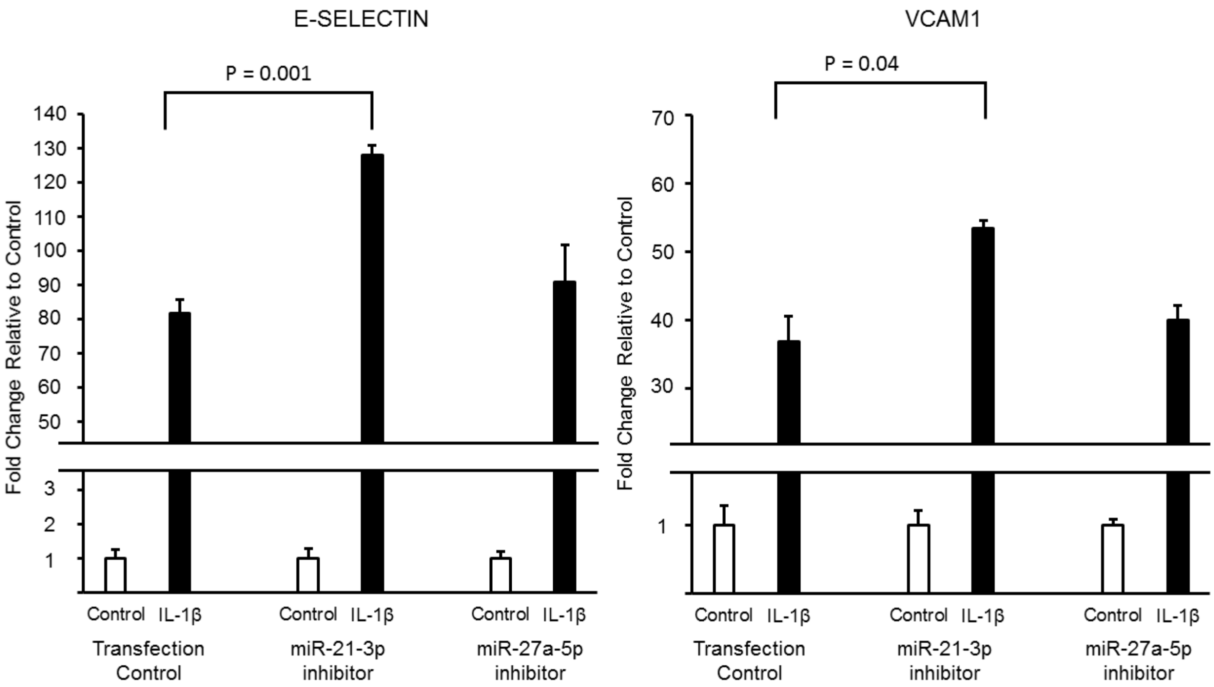
Supplementary Figure III: Transient over-expression of miR-21-3p and miR-27a-5p in HAECs. Cells were transfected with either miR-21-3p or miR-27a-5p mimic at 1nM concentration for 24 hours. miRNA expression was quantified using RT-qPCR to determine the level of over-expression. N = 3 for each donor, bars represent +/- SEM.



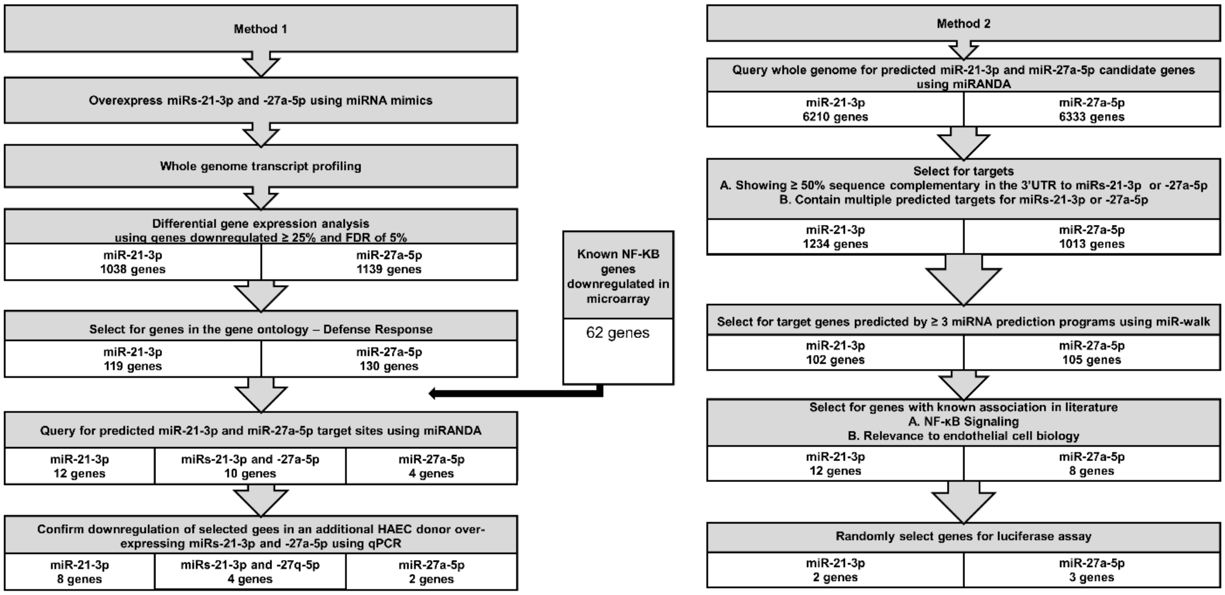
B

Condition	Control	Ox-PAPC	IL-1β
p65/ Lamin A/C	0.18	0.04	1.73

Supplementary Figure IV. Effects of Ox-PAPC treatment on p65 nuclear translocation in HAECs. **A.** HAECs were transfected with 1nM control, miR-21-3p or miR-27a-5p mimic for 24 hours and then treated with 40μg/mL Ox-PAPC for four hours or 20ng/mL IL-1β (as a positive control) for two hours. Nuclear p65 was quantified with Western blots. **B.** Densitometric quantification of p65 expression relative to Lamin A/C.



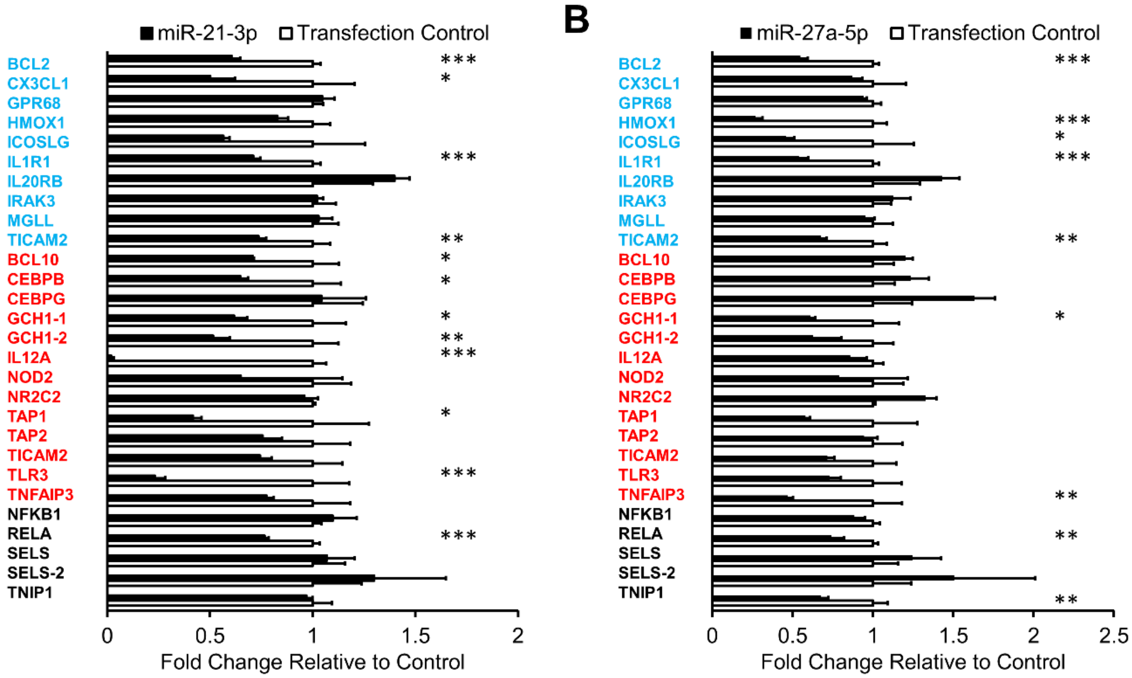
Supplementary Figure V. Expression of E-selectin and VCAM1 in HAECs upon IL-1B treatment following repression of miRs-21-3p and -27a-5p. Cells were transfected with either miR-21-3p or miR-27a-5p inhibitor at 50nM concentration. 24 hours post-transfection cells were treated with 2ng/mL IL-1β for two hours. mRNA expression was quantified using RT-qPCR. N = 3 for each donor, bars represent +/- SEM.



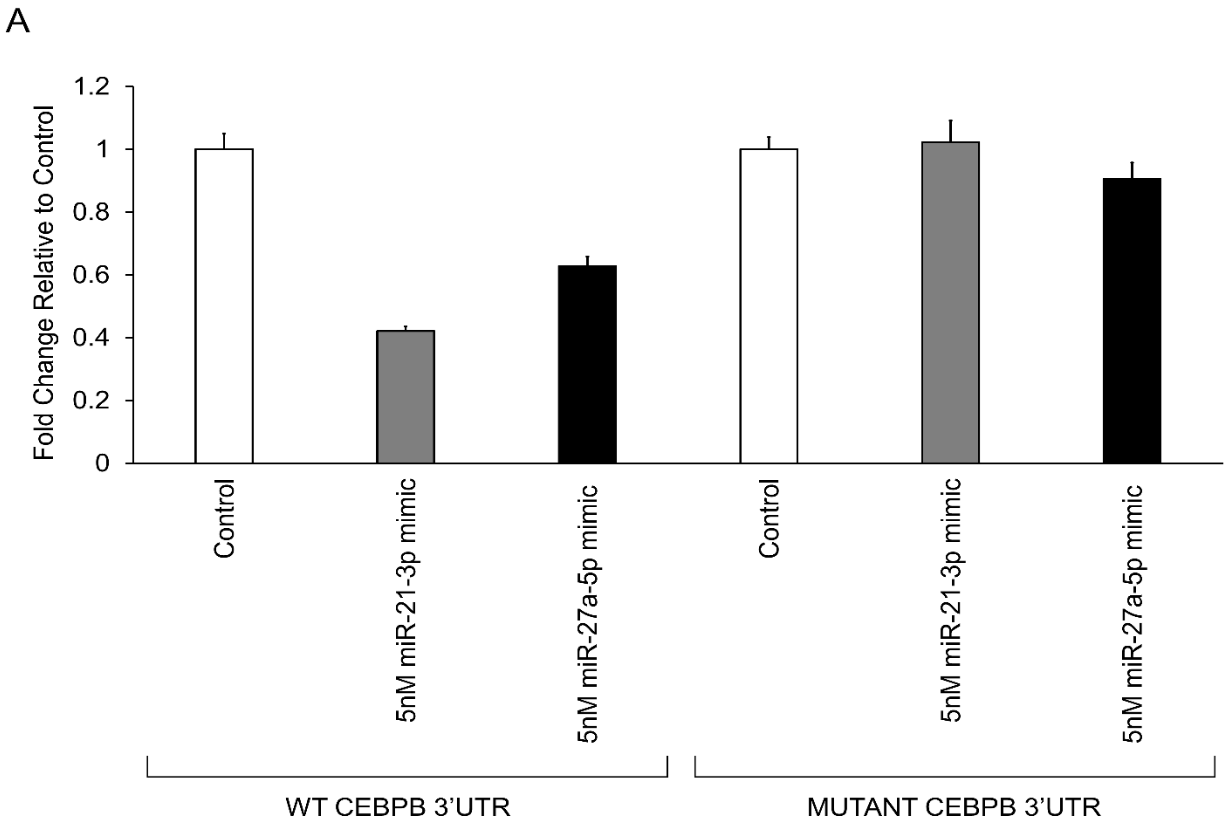
Final List of Candidate miR-21-3p and miR-27a-5p candidate genes

Method 1			Method 2		
miR-21-3p	**miRs -21-3p and -27a-5p**	**miR-27a-5p**	**miR-21-3p**	**miRs -21-3p and - 27a-5p**	**miR-27a-5p**
BCL10	BCL2	RELA	CBX4	MAP2K7	RFC1
CEBPB	HMOX1	TNIP1	HMGB1	UBE2N	
CX3CL1	ICOSLG				
GCH1	TICAM2				
IL12A					
TAP1					
TLR3					
TNFAIP3					

Supplementary Figure VI. Workflow for each in silico method used to identify candidate target genes of miRs-21-3p and -27a-5p.



Supplementary Figure VII: Expression of candidate target genes in response to miRNA over-expression. **A** and **B**. HAECs were transfected with either miR-21-3p mimic or miR-27a-5p mimic at 50nM concentration for 24 hours. Gene expression was measured by RT-qPCR for 26 putative candidate genes from the Gene Ontology category defense response predicted to have miRNA binding sites by miRANDA. Panel **A** shows the results for the miR-21-3p mimic transfected HAECs and panel B shows the results for the miR-27a-5p mimic transfected cells. For panels **A** and **B**: Blue color indicates genes that are predicted to be miR-21-3p and miR-27a-5p targets. Red color indicates genes that are predicted to be miR-21-3p targets. Black color indicates genes that are predicted to be miR-27a-5p targets. SELS and SELS-2, GCH1-1 and GCH1-2 represent two different isoforms of the same gene, SELS and GCH1, respectively. Bars indicate average +/- SEM. N = 3.



B

```
    3’-ugucGGGUAGCUGACCACAAc-5’ hsa-miR-21-3p
           |||: | : |||||||
207:5’-ggcuCCCGCCCGU-GGUGUUa-3’ WT CEBPB – miR-21-3p predicted target site
         | |  ||  || :|: :|
  3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p
                                      ⬇

     3’-ugucGGGUAGCUGACCACAAc-5’ hsa-miR-21-3p
            |||: | :
 207:5’-ggcuCCCGCCCGA-AAAAAAa-3’ CEBPB – miR-21-3p mutated target site
          | |  ||     |
   3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p
```

Supplemental Figure VIII: Loss of predicted miR-21-3p target site leads to impaired targeting of *CEBPB* 3’UTR by miRs-21-3p and -27a-5p. **A**. For each gene, a plasmid containing 3’UTR of *CEBPB* with either the miRANDA predicted (WT) or mutated 21-3p target site was co-transfected with miRNA mimic at 5nM concentration in HEK293 cells. Bars represent average +/- SD. N = 6. **B.** Predicted interactions of miRs-21-3p and -27a-5p with *CEBPB* 3’UTR.

Supplementary Table I: Mapping Statistics for next generation sequencing of HAEC small RNAs. Small RNA isolated from two EC donors were sequenced using the Illumina GAIIx platform and aligned to the hg19 version of the genome using the Novoalign. Unique miRNA identified was determined by the presence of at least ten reads in a given library mapped to the miRNAs' sequence

	Donor 1		Donor 2	
	Control	**OxPAPC**	**Control**	**OxPAPC**
Number of total reads	15,037,715	19,293,486	26,189,339	21,215,273
Number of reads aligned to miRNA regions in the genome	8,460,708	7,771,730	15,533,950	13,254,925
Number of uniquely aligned reads to miRNA regions in the genome	7,078,025	5,613,510	11,202,433	9,811,971
Number of unique miRNAs detected	386	434	583	560

Supplementary Table II: miR-27a-5p complementary sites within predicted miR-21-3p sites. miRNA-mRNA interaction is the physical representation of the given miRNA with its target mRNA. miR-21-3p interactions were generated by the miRANDA algorithm, while miR-27a-5p alignments with hsa-miR-21-3p predicted target sites were generated by visual inspections. Watson-Crick indicates the number of Watson-Crick base pairs in the given alignment between the miRNA and mRNA. Wobble indicates the number of wobble base pairs in the given alignment. Total number of commentary bases is the sum of both Watson-Crick and Wobble bases in a given alignment.

I. miR-21-3p target site in miR-21-3p positive control				
miRNA-mRNA interaction	miRNA	Watson - Crick	Wobble	Total number of complementary bases

`              3’-UGUCGGGUAGCUGACCACAAC-5’ hsa-miR-21-3p`
`                 |||||||||||||||||||||`
`              5’-ACAGCCCAUCGACUGGUGUUG-3’ hsa-miR-21-3p target sequence`
`                   ||||| |`
`3’-ACGAGUGUUCGUCGAUUCGGG-A-5’ hsa-miR-27a-5p`
	miR-21-3p	21	0	21

	miR-27a-5p	6	0	6
II. miR-21-3p target sites in genes only predicted to be targeted by miR-21-3p				

`      3’-ugucggguagcugaCCACAAc-5’ hsa-miR-21-3p`
`                       ||||||`
`  913:5’-auuuuuguagagacGGUGUUu-3’ BCL10 – miR-21-3p predicted target site 1`
`             : |: :|| |`
`3'-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p`
	miR-21-3p	6	0	6

	miR-27a-5p	4	3	7
`     3’-ugUCGGGUAGCUGACCACAAc-5’ hsa-miR-21-3p` ` |||		|||||||` `1624:5‘-auAGCAAAAAUAGUGGUGUUa-3’ BCL10 – miR-21-3p predicted target site 2` ` :|||	:|: :|` ` 3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p`	miR-21-3p	12	0	12
	miR-27a-5p	6	4	10

<table>
<tr><td rowspan="2">3’-ugucGGGU-AGC-UG-ACCACAAc-5’ hsa-miR-21-3p
|||: |:| || |||||||
39:5’-uacuCCCGUUUGUACGUGGUGUUa-3’CBX4 - miR-21-3p predicted target site
|| ||| |
3’-ACGAGUGUUCGUCGAUUCGGG-A-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>14</td><td>2</td><td>16</td></tr>
<tr><td>miR-27a-5p</td><td>6</td><td>0</td><td>6</td></tr>
<tr><td rowspan="2">3’-ugucGGGUAGCUGACCACAAc-5’ hsa-miR-21-3p
|||: | : |||||||
207:5’-ggcuCCCGCCCGU-GGUGUUa-3’ CEBPB - miR-21-3p predicted target site
| | || || :|: :|
3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>11</td><td>2</td><td>13</td></tr>
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|| |:| :| |||||||
531:5’-ugAGGCUAGUG—UGGUGUUu-3’ CX3CL1 - miR-21-3p predicted target site
:| ||:: |:: ::|
3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>12</td><td>2</td><td>14</td></tr>
<tr><td>miR-27a-5p</td><td>5</td><td>7</td><td>12</td></tr>
<tr><td rowspan="2">3’-ugucggguagcuGACCACAAc-5’ hsa-miR-21-3p
||||||||
639:5' gggaauuaguucCUGGUGUUg 3' GCH1 - miR-21-3p predicted target
| : | ||::| |
3’-ACGAGUGUUCGUCGAUUCGGG-A-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>8</td><td>0</td><td>8</td></tr>
<tr><td>miR-27a-5p</td><td>6</td><td>3</td><td>9</td></tr>
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:|| | :|||||||
2093:5’-gauuagUAUGGUUUGGUGUUc-3’ HMGB1 - miR-21-3p predicted target site
: : || ||::|
3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>10</td><td>2</td><td>12</td></tr>
<tr><td>miR-27a-5p</td><td>5</td><td>4</td><td>9</td></tr>
<tr><td rowspan="2">3’ ugucGGGUAG---CUGACCACAAc-5’ hsa-miR-21-3p
:||||| || ||||||
203:5’-aauaUCCAUCC-UGA-AGGUGUUu-3’ IL12A - miR-21-3p predicted target site
: : || | |:|: ::|
3’-ACGAGUGUUCGUCGA-UUCG-GGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>13</td><td>1</td><td>14</td></tr>
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|:|||||||
346:5’-uuuauaauaaaAUUGGUGUUu-3’ TAP1 - miR-21-3p predicted target site
| : :|| | | : : |:::
3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>8</td><td>1</td><td>9</td></tr>
<tr><td>miR-27a-5p</td><td>6</td><td>7</td><td>13</td></tr>
<tr><td rowspan="2">3’-ugucggguagcugaCCACAAc-5’ hsa-miR-21-3p
||||||
67:5’-aaguuuuccauaaaGGUGUUa-3’ TLR3 - miR-21-3p predicted target site
: || |:|: :|
3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>6</td><td>0</td><td>6</td></tr>
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</table>

<table>
<tr><td rowspan="2">3’-ugUCGGGUAGCUGACC-ACAAc-5’ hsa-miR-21-3p
| ||::|: |||| ||||
877:5’-auAACCUGUUUUCUGGUUGUUg-3’ TNFAIP3 – miR-21-3p predicted target site
| | ||: ::||
3’-ACGAGUGUUCGUCGAUUCGGGA-5’ has-miR-27a-5p</td><td>miR-21-3p</td><td>12</td><td>3</td><td>15</td></tr>
<tr><td>miR-27a-5p</td><td>6</td><td>3</td><td>9</td></tr>
<tr><td colspan="5">III. miR-21-3p target sites in genes predicted to be targeted by miRs-21-3p and -27a-5p</td></tr>
<tr><td rowspan="2">3’-ugucggguagcugaCCACAAc-5’ hsa-miR-21-3p
||||||
461:5’-gaggcuggggagaaGGUGUUc-3’ BCL2 – miR-21-3p predicted target site
:| :| : |:|: :|
3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>6</td><td>0</td><td>6</td></tr>
<tr><td>miR-27a-5p</td><td>5</td><td>6</td><td>11</td></tr>
<tr><td rowspan="2">3' ugucggguagcugaCCACAAc 5' hsa-miR-21-3p
||||||
527:5' uggguggggagggaGGUGUUu 3' HMOX1 – miR-21-3p predicted target site
::| :| :: ::|
3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>6</td><td>0</td><td>6</td></tr>
<tr><td>miR-27a-5p</td><td>3</td><td>7</td><td>10</td></tr>
<tr><td rowspan="2">3’-ugucgggUAGCUGACCACAAc-5’ hsa-miR-21-3p
| ||| ||||||
367:5’-uccugagACCGAAGGGUGUUu-3’ ICOSLG – miR-21-3p predicted target site – 1
| || | | | : |:::
3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>10</td><td>0</td><td>10</td></tr>
<tr><td>miR-27a-5p</td><td>7</td><td>4</td><td>11</td></tr>
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|| || | |||||||
1544:5’-uuAGAAGAU-GUGUGGUGUUu-3’ ICOSLG – miR-21-3p predicted target site – 2
| | | |: : |:::
3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>12</td><td>0</td><td>12</td></tr>
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:||:: | | |||||||||
1772:5’-cuGGCUUCUAGUCUGGUGUUc-3’ IL1R1 – miR-21-3p predicted target site
| :| ||:|:
3’-ACGAGUGUUCGUCGAUUCGGGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>12</td><td>3</td><td>15</td></tr>
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||||||
678:5’-auuguacuugguggGGUGUUu-3’ MAP2K7 – miR-21-3p predicted target site – 1
| ::| ::|: ::|:::
3’-ACGAGUGUUCGUCG-AUUCGGGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>6</td><td>0</td><td>6</td></tr>
<tr><td>miR-27a-5p</td><td>4</td><td>10</td><td>14</td></tr>
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||: |: :: ||||||
1273:5’-guuuCCUUUUUGUGGGUGUUg-3’ MAP2K7– miR-21-3p predicted target site – 2
| | : |::|: ::
3’-ACGAGUGUUCGUCGAUUCG-GGA-5’ hsa-miR-27a-5p</td><td>miR-21-3p</td><td>9</td><td>4</td><td>13</td></tr>
<tr><td>miR-27a-5p</td><td>4</td><td>6</td><td>10</td></tr>
</table>

3'-ugUCGGGU-AGCUG----ACCA-CAAc-5' hsa-miR-21-3p |||||| |:||: |||| ||| 621:5'-acAGCCCAUUUGAUAGUGUGGUAGUUa-3' TICAM2 - miR-21-3p predicted target site - 1 | ||||| 3'-ACGAGUGUUCGUCGAU-UCGGGA-5' hsa-miR-27a-5p	miR-21-3p	16	2	18
	miR-27a-5p	6	0	10
3'-ugUCGGGUAGCUGACCACAAc-5' hsa-miR-21-3p | ::|:| || |||||||| 649:5'-ggACUUCGUGGAGUGGUGUUc-3' TICAM2- miR-21-3p predicted target site - 2 : |::| :|: :| 3'-ACGAGUGUUCGUCGAUUCGGGA-5' hsa-miR-27a-5p	miR-21-3p	12	3	15
	miR-27a-5p	4	5	9
3'-ugucggguagcugaCCACAAc-5' hsa-miR-21-3p |||||| 320:5'-gcugcaggggugugGGUGUUu-3' UBE2N - miR-21-3p predicted target site ::||:| : |::|: ::| 3'-ACGAGUGUUCGUCGAUUCG-GGA-5' hsa-miR-27a-5p	miR-21-3p	6	0	6
	miR-27a-5p	6	9	13