Supplementary figure legends:

Figure S1. Highly significant correlation between libraries in A) normoxia and B) hypoxia. Read counts obtained by deep-sequencing of the libraries were log10 transformed and compared. Both normoxic and hypoxic libraries show a highly significant correlation (Pearson's r=-0.96, *p*-value <0.0001).

Figure S2. Alternative arm-selection. Sequences of 3 annotated mature miRNA/miRNA* pairs displaying unexpected ratios in endothelial cells. For these miRNAs, the annotated Star sequence showed a >5- times higher expression than its annotated mature sibling.

Figure S3. Novel miRNA* sequences. For each of the 9 newly identified miRNA*, the predicted secondary structure of the miRNA stem-loop and its genomic location are indicated; within the stemloop, the novel miRNA* is highlighted in red, while the corresponding mature sequences is indicated in blue. Moreover, both the mature miRNA and the miRNA* sequences (in bold) are indicated, along with the average read counts found in all four libraries. In agreement with miRBase v18.0 nomenclature, we indicated the mature miRNA and miRNA* species according to their location on the hairpin (-5p or -3p).

Figure S4. MiRNAs display a great variety in length. Bar graphs representing length variations at the 5'-end (A) and at the 3'-end (B). Average values of the 4 libraries are shown.

Figure S5. Sequence and length variations of 33 annotated mature human miRNAs. The annotated mature sequences are in bold, seed-regions are shown within a black rectangle. Mismatches due to SNPs or editing-events are highlighted in yellow, deletions are shown as hyphens and additional nucleotides are in red. Hits are average values of the 2 normoxic- and hypoxic-libraries. All variants were intersected with miRBase deep sequencing data: **A)** Sequence and length variations for

which we and others identified the same isomiRs variation as the highest expressed sequence; **B)** Sequence and length variations described as the most abundant by us only.

Figure S6. Library composition. Pie chart of distribution of reads mapping one (blue), two or three (red) or multiple times (green) to the human genome, identified by overlap with miRBase and small RNA annotations included in DeepBase: small RNA originating from long non-coding RNA (nasRNA), promoter-associated small RNA (pasRNA), exon-associated small RNA (easRNA), repeat-associated small RNA (rasRNA) and small nucleolar RNA (snoRNA).

Figure S7. Northern Blotting of novel-181 and novel-1322. Total RNA of HUVEC was fractionated on 15% polyacrylamide denaturing gel and blotted. miRNAs were detected using complementary LNA-probes.

Figure S8. Predicted stem-loops of novel-miRNAs. Hairpins of the 18 novel miRNAs, folded by RNAfold tool (Vienna RNA package). Nucleotides with red background indicate the identified mature sequences; nucleotides with blue background, when present, indicate potential star sequences. Additionally, information about genomic location and context, values of free energy and conservation.

Figure S9. Differential miRNA expression upon hypoxia. Levels of novel-112, novel-144 and hsa-miR-210 were measured by qPCR in HUVEC exposed to 1% oxygen for 24 or 48 hrs.
At both timepoints, novel-112 and novel-144 miRNAs were down modulated and miR-210 was induced (n=8; * $p<0.05$; ** $p<0.001$; *** $p<0.001$).

Table S1. Annotated miRNAs. Raw counts and their relative percentages in each library are indicated for annotated miRNAs. On the left (> 0.001% counts), readily detectable miRNAs are indicated, i.e. miRNA exhibiting more than 0.001% counts in both normoxic libraries. On the right, barely detectable miRNAs are shown (0.0001% - 0.001% counts). These miRNA displayed at least one read in each library, but also had less than 0.001% counts in one or both normoxic libraries.

Table S2. Characteristcs of isomiRs in endothelial cells.

Table S3. miRNA candidates. Candidate miRNAs are shown, ordered by chromosome number and position. Genomic location, sequence, and number of reads are shown for each candidate miRNA species. Some of them (e.g. novel-1113-1 and novel-1113-2) display the same mature sequence and are likely paralog miRNAs. Genomic location, length and calculated free energy of the corresponding predicted hairpins are also shown, as well as the genomic context. Candidates miRNAs that underwent experimental validation are highlighted in grey.

Figure S1 A

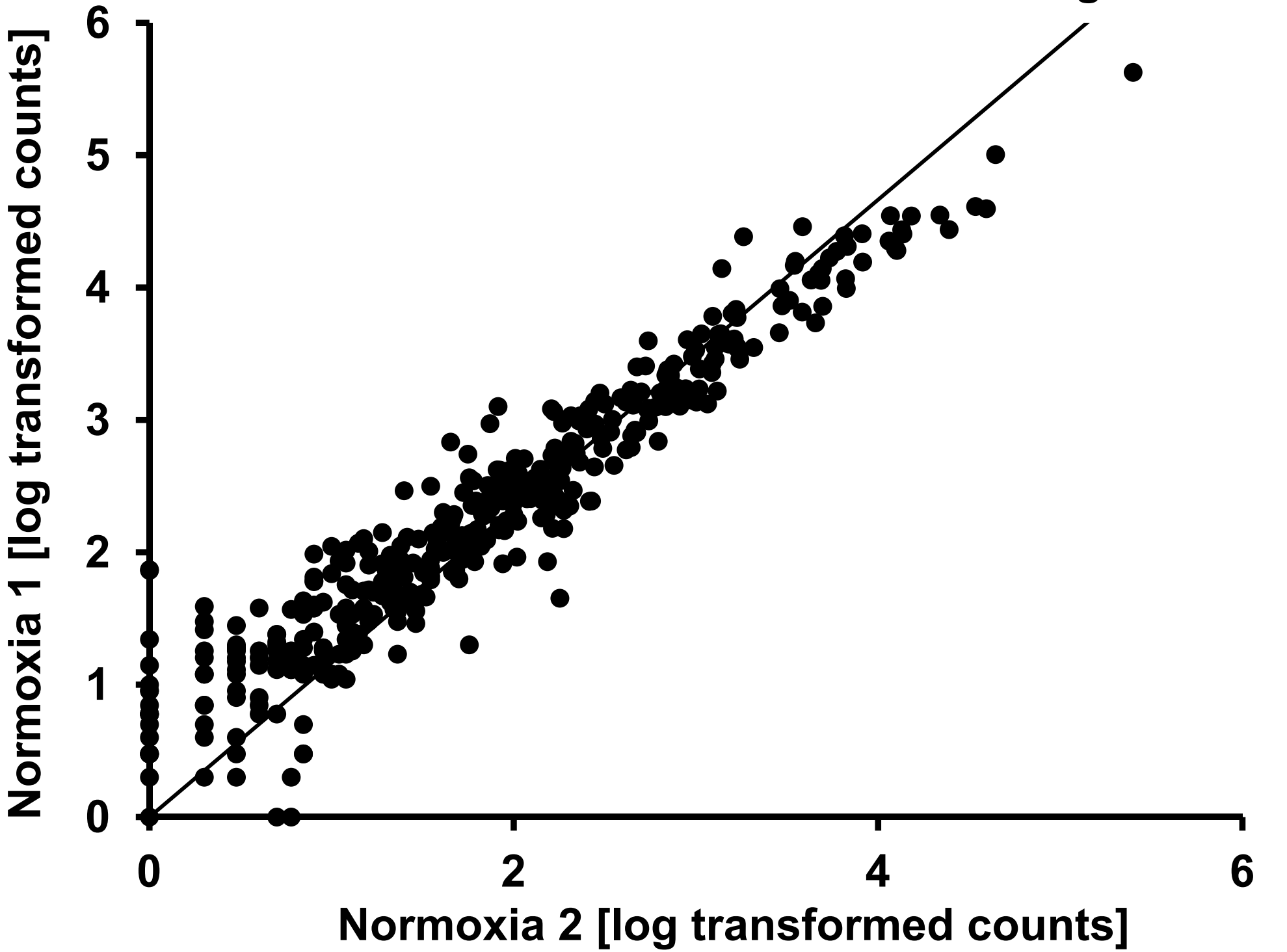
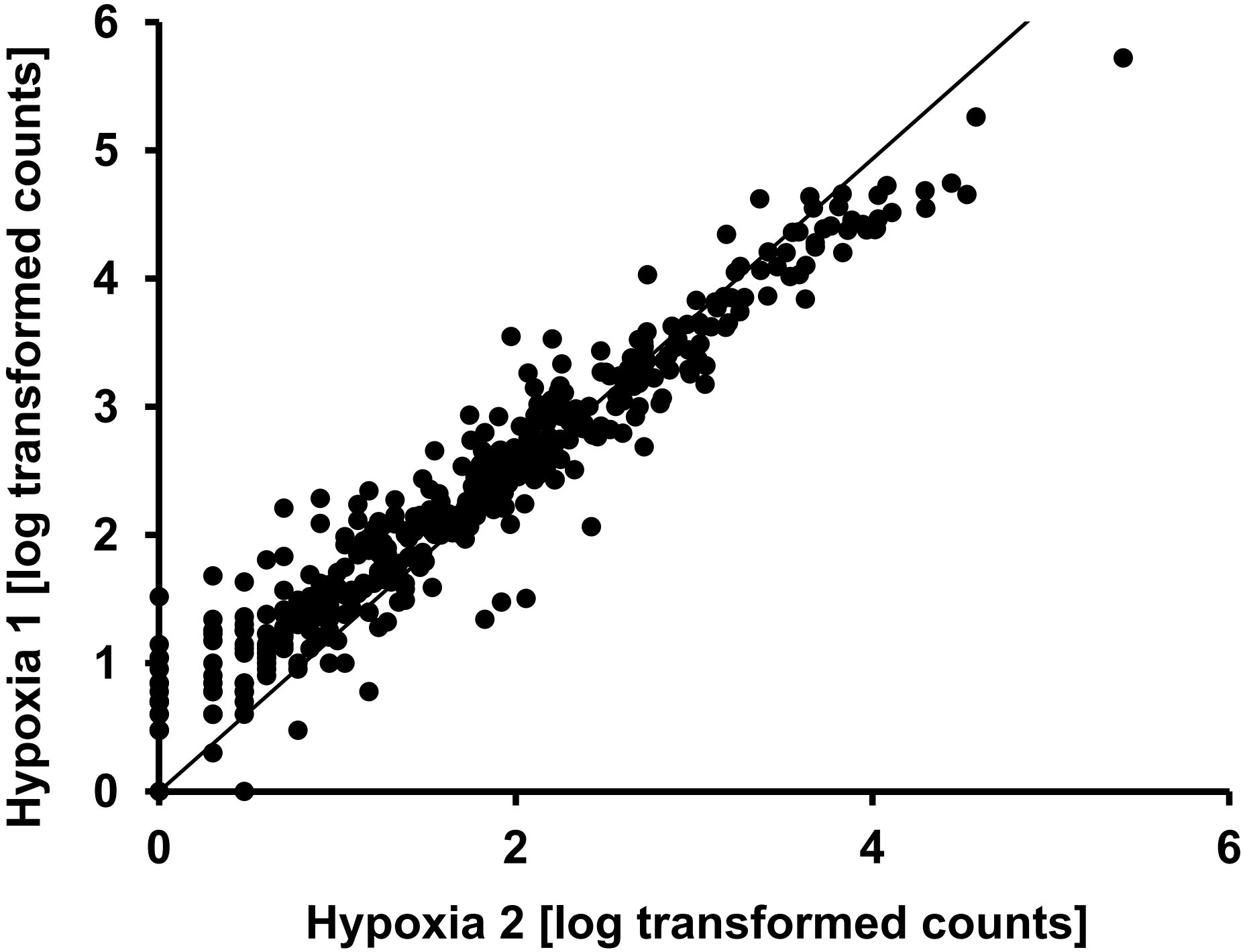

Normoxia 1 [log transformed counts]
0
1
2
3
4
5
6
0
2
4
6
Normoxia 2 [log transformed counts]

Figure S1 B


Hypoxia 1 [log transformed counts]
0
1
2
3
4
5
6
0
2
4
6
Hypoxia 2 [log transformed counts]

Alternative Arm selection

Figure S2

hsa-miR-214-5p	hsa-miR-214-3p	Counts
star	mature	
..UGCCUGUCUACACUUGCUGUGC.....		507
.....	ACAGCAGGCACAGACAGGCAGU.....	92

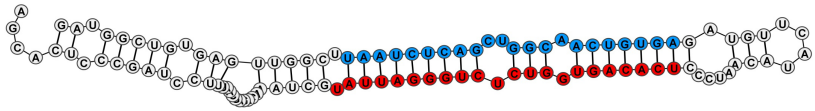
hsa-miR-33a-5p	hsa-miR-33a-3p	Counts
mature	star	
....GUGCAUUGUAGUUGCAUUGCA.....		33
.....	CAAUGUUUCCACAGUGCAUCAC	176

hsa-miR-616-5p	hsa-miR-616-3p	Counts
star	mature	
.....ACUCAAAACCCUUCAGUGACUU		18
.....	AGUCAUUGGAGGGUUUGAGCAG	2

Figure S3

hsa-mir-216a, chr2: 56216085-56216194 [-]

miR-216a-5p (Mature) 19 - uaaucucagcuggcaacuguga - 40 Counts: 636

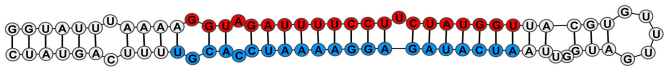


miR-216a-3p (Star) **58 - ucacaguggucucugggauuau - 79** **Counts: 76**

---

hsa-mir-376a-2, chr14: 101506406-101506485 [+]

miR-376a-2-5p (Star) **12 - gguagauuuuccuucuauggu - 32** **Counts: 18**

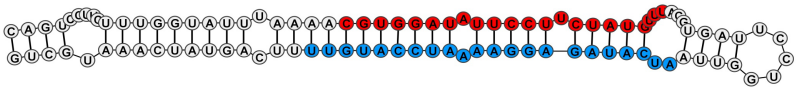


miR-376a-3p (Mature) 50 - aucauagaggaaaauccacgu - 70 Counts: 1404

---

hsa-mir-376b, chr14: 101506773-101506872 [+]

miR-376b-5p (Star) **23 - cguggauauuccuucuauguuu - 45** **Counts: 16**

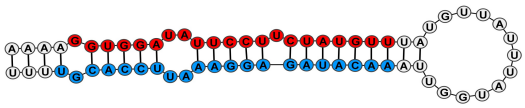


miR-376b-3p (Mature) 62 - aucauagaggaaaauccauguu - 83 Counts: 1717

---

hsa-mir-376c, chr14: 101506027-101506092 [+]

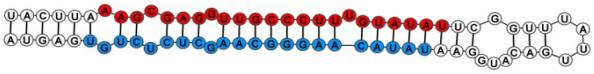
miR-376c-5p (Star) **5 - gguggauauuccuucuauguu - 25** **Counts: 53**



miR-376c-3p (Mature) 43 - aacauagaggaaauuccacgu - 63 Counts: 6248

hsa-mir-381, chr14: 101512257-101512331 [+]

miR-381-5p (Star) **7 - aagcgagguugcccuuuguauau - 30** **Counts: 55**

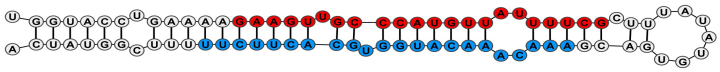


miR-381-3p (Mature) 49 - uauacaagggcaagcucucugu - 70 Counts: 385

---

hsa-mir-495, chr14: 101500092-101500173 [+]

miR-495-5p (Star) **14 - gaaguugcccauguuauuuucg - 35** **Counts: 13**



miR-495-3p (Mature) 50 - aaacaaacauggugcacuucuu - 71 Counts: 517

---

hsa-mir-503, chrX: 133680358-133680428 [-]

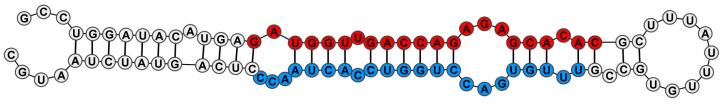
miR-503-5p (Mature) 6 - uagcagcgggaacaguucugcag - 28 Counts: 411

miR-503-3p (Star) **46 - gggguauuguuuccgcugccagg - 68** **Counts: 66**

---

hsa-mir-758, chr14: 101492357-101492444 [+]

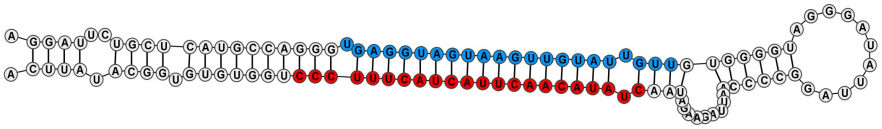
miR-758-5p (Star) **15 - gaugguugaccagagagcacac - 36** **Counts: 39**



miR-758-3p (Mature) 52 - uuugugaccugguccacuaacc - 73 Counts: 57

hsa-mir-98, chr:X:53583184-53583302 [-]

miR-98-5p (Mature) 22 - ugagguaguaaguuguauuguu - 43 Counts: 1018



miR-98-3p (Star) **80 - cuauacaacuuacuacuuuccc - 101** **Counts: 52**

Figure S4

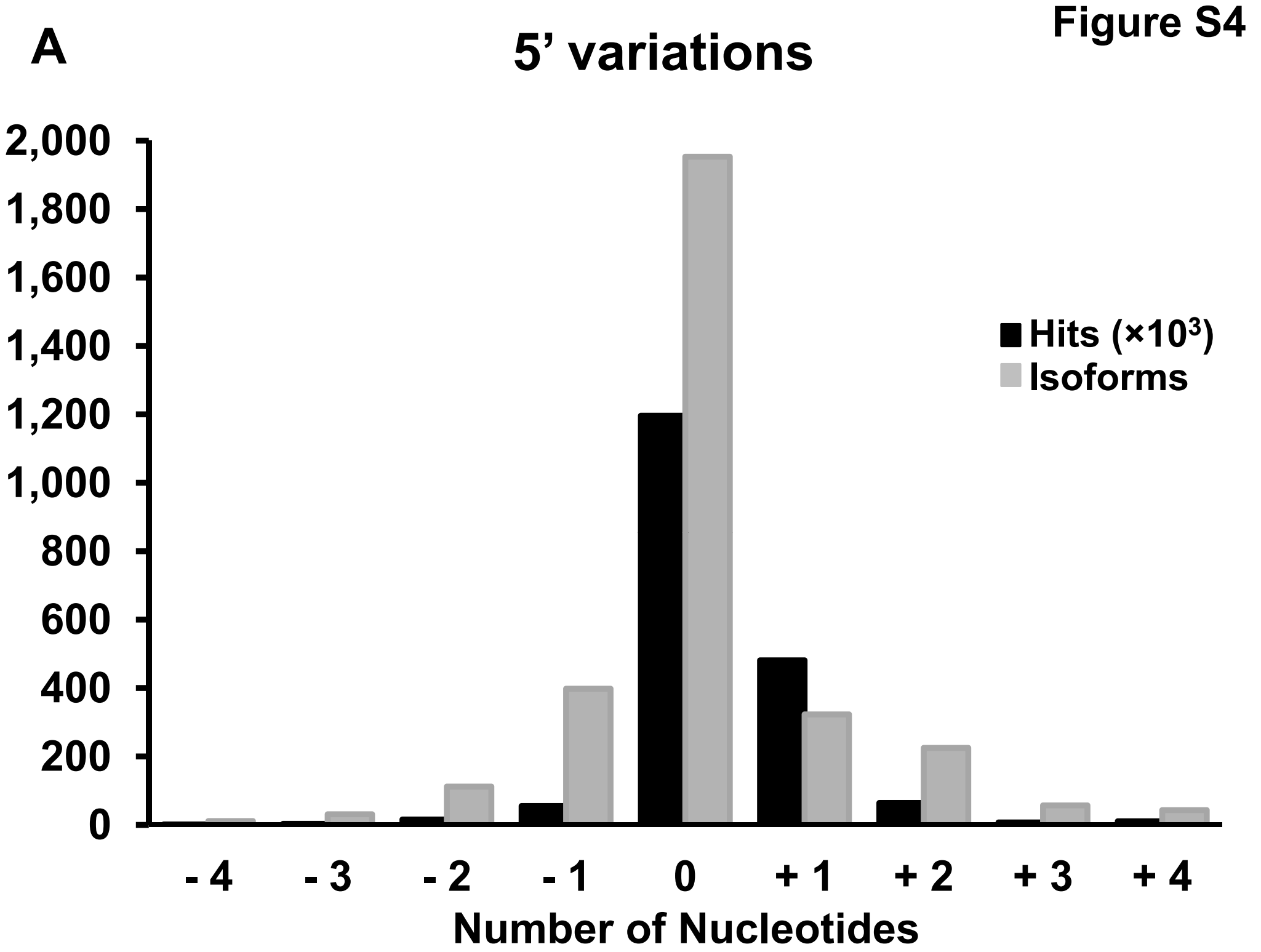

A
5’ variations
2,000
1,800
1,600
1,400
1,200
1,000
800
600
400
200
0
Hits (×10³)
Isoforms
- 4
- 3
- 2
- 1
0
+ 1
+ 2
+ 3
+ 4
Number of Nucleotides

Figure S4

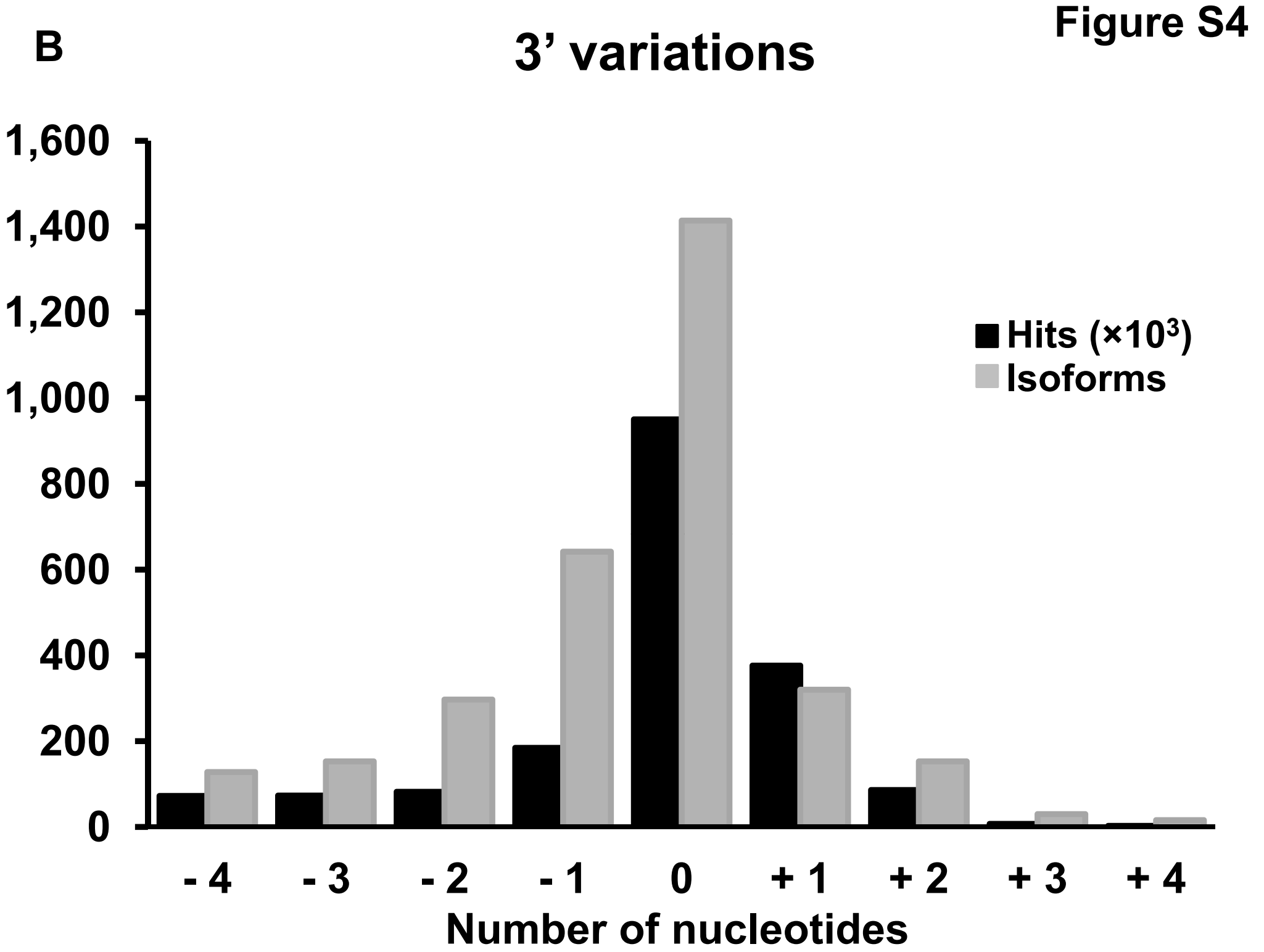

B
3’ variations
1,600
1,400
1,200
1,000
800
600
400
200
0
Hits (×10³)
Isoforms
- 4
- 3
- 2
- 1
0
+ 1
+ 2
+ 3
+ 4
Number of nucleotides

Figure S5 A

hsa-miR-10b-5p, chr2:177015057-177015079[+]	Normoxic	Hypoxic
UACCCUGUAGAACCGAAUUUGU-	786	1458
UACCCUGUAGAACCGACUUUGU-	242	411
UACCCUGUAGAACCGAAU-----	240	382
-ACCCUGUAGAACCGAAUUUGUG	204	445
UACCCUGUAGAACCGAA------	157	235
UACCCUGUAGAACCGAAUUUGUG	148	296
UACCCUGUAGAACCGAACUUGU-	129	241
UACCCUGUAGAACCGAAUCUGU-	129	236
-ACCCUGUAGAACCGACUUUGU-	89	159
-ACCCUGUAGAACCGAAUUUGU-	85	216

hsa-miR-21-5p, chr17:57918634-57918655[+]	Normoxic	Hypoxic
UAGCUUAUCAGACUGAUGUUGAC	210948	243650
UAGCUUAUCAGACUGAUGUUGA	28170	38222
UAGCUUAUCAGACUGAUGU---	17391	18740
UAGCUUAUCAGACUGAUGUUG-	14675	17241
GGUAGCUUAUCAGACUGAUGUUGAC	14027	18233
UAGCUUAUCAGACUGAUG----	13433	13680
UAGCUUAUCAGACUGAUGCUGAC	8321	9108
UAGCUUAUCAGACUGAGGUUGA	6426	8498
UAGCUUAUCAGACUGACGUUGA	6238	8543
UAGCUUAUCAGACUGAUGAUGAC	5783	6232

hsa-miR-27a-3p, chr19:13947261-13947281[-]	Normoxic	Hypoxic
UUCACAGUGGCUAAGUUCCG-	3714	4767
UUCACAGUGGCUAAGUUCCGC	1772	2107
UUCACAGUGGCUAAGUUCC--	1545	1874
UUCACAGUGGCUAAGAUCCGC	636	816
UUCACAGUGGCUAAGCUCCGC	327	341
UUCACAGUGGCUAAGUACCG-	240	296
UUCACAGUGGCUAAGGUCCGC	183	207
UUCACAGUGGCUAAGUCCCG-	178	204
UUCACAGUGGCUAAGUGCCG-	95	127
UUCACAGUGGCUAAGUACCGC	95	108

hsa-miR-30a-5p, chr6:72113298-72113319[-]	Normoxic	Hypoxic
UGUAAACAUCCUCGACUGGAAGCU	16150	27976
UGUAAACAUCCUCGACUGGAAGC	3383	5438
UGUAAACAUCCUCGACUGGAAACU	991	1204
UGUAAACAUCCUCGACUGAAAGCU	528	651
UGUAAACAUCCUCGACUGGA--	523	681
UGUAAACAUCCUCGACUGG---	521	621
UGUAAACAUCCUCGACU-----	508	495
UGUAAACAUCCUCGACUGGAA-	484	680
UGUAAACAUCCUCGACUGGAAG	478	852
-GUAAACAUCCUCGACUGGAAGCU	469	795

hsa-miR-30c-5p, chr1:41222972-41222994[+], chr6:72086706-72086728[-]	Normoxic	Hypoxic
UGUAAACAUCCUACACUCUCAGCU	2096	2816
UGUAAACAUCCUACACUCUC---	1378	1163
UGUAAACAUCCUACACUCUCAGC	1001	1138
UGUAAACAUCCUACACUCU----	785	690
UGUAAACAUCCUACACUCUCAG-	743	942
UGUAAACAUCCUACACUC-----	693	704
UGUAAACAUCCUACACUCUCA--	509	398
UGUAAACAUCCUACACUCUCAACU	342	435
UGUAAACAUCCUACAC-------	330	334
UGUAAACAUCCUACACUCACAGCU	204	184

hsa-miR-30d-5p, chr8:135817162-135817183[-]	Normoxic	Hypoxic
UGUAAACAUCCCCGACUGGAAGCU	4576	9417
UGUAAACAUCCCCGACUGGAAGC	1020	1988
UGUAAACAUCCCCGACUGGAAACU	316	611
UGUAAACAUCCCCGACUGGAAG	163	313
UGUAAACAUCCCCGACUGAAAGCU	162	327
UGUAAACAUCCCCGACUGGGAGCU	160	262
UGUAAACAUCCCCGACUGG---	144	190
UGUAAACAUCCCCGACUGGA--	135	195
UGUAAACAUCCCCGACUGGAA-	133	229
UGUAAACAUCCCCGACU-----	98	147

hsa-miR-30e-5p, chr1:41220043-41220064[+]	Normoxic	Hypoxic
UGUAAACAUCCUUGACUGGAAGCU	1587	2331
UGUAAACAUCCUUGACUGGAAGC	265	342
-GUAAACAUCCUUGACUGGAAGCU	147	247
UGUAAACAUCCUUGACUGGAAACU	80	78
UGUAAACAUCCUUGACUGAAAGCU	46	48
-GUAAACAUCCUUGACUGGAAGC	44	51
UGUAAACAUCCUUGACUGGAA-	39	28
UGUAAACAUCCUUGACUGGAAG	36	46
UGUAAACAUCCUUGACUGG---	29	24
-GUAAACAUCCUUGACUGGAAGCUGU	23	28

hsa-miR-31-5p, chr9:21512157-21512177[-]	Normoxic	Hypoxic
AGGCAAGAUGCUGGCAUAGCUGU	6352	8222
AGGCAAGAUGCUGGCAUAGCUG	6828	7433
AGGCAAGAUGCUGGCAUAGCU	3402	4531
AGGCAAGAUGCUGGCAUAGC-	2403	2383
AGGCAAGAUGCUGGCAUAG--	1779	1840
AGGCAAGAUGCUGGCAAAGCUG	1742	1659
AGGCAAGAUGCUGGCAU----	1500	1274
AGGCAAGAUGCUGGCAUCGCUGU	1178	1383
AGGCAAGAUGCUGGCAUTGCUGU	1178	1303
AGGCAAGAUGCUGGCAUGGCUGU	1146	1319

hsa-miR-181b-5p, chr9:127456004-127456026[+], chr1:198828054-198828076[-]	Normoxic	Hypoxic
AACAUUCAUUGCUGUCGGUGGGUU	1666	2967
AACAUUCAUUGCUGUCGGUGGG-	932	1504
AACAUUCAUUGCUGUCGGUGGGUUG	740	1219
AACAUUCAUUGCUGUCGGUGGGU	639	1010
AACAUUCAUUGCUGUCGGUGG--	364	460
AACAUUCAUUGCUGUCGGCGGGUU	292	460
AACAUUCAUUGCUGUCGGU----	286	367
-ACAUUCAUUGCUGUCGGUGGGUU	248	266
AACAUUCAUUGCUGUCGGAGGGUU	242	368
AACAUUCAUUGCUGUCGG-----	228	244

hsa-miR-221-3p, chrX:45605608-45605630[-]	Normoxic	Hypoxic
AGCUACAUUGUCUGCUGGGUUU-	8788	9656
AGCUACAUUGUCUGCUGGGUUUC	6015	6004
AGCUACAUUGUCUGCUGGGU---	3590	3448
AGCUACAUUGUCUGCUGGGUU--	3392	3508
AGCUACAUUGUCUGCUGGG----	2301	2154
AGCUACAUUGUCUGCUGGGUAUC	943	845
AGCUACAUUGUCUGCUGGGCUUC	895	821
AGCUACAUUGUCUGCUGG-----	788	709
AGCUACAUUGUCUGCUGGGAUUC	750	756
AGCUACAUUGUCUGCUGGGCUU-	621	639

hsa-miR-222-3p, chrX:45606442-45606462[-]	Normoxic	Hypoxic
AGCUACAUCUGGCUACUGGGUCU	4627	7828
AGCUACAUCUGGCUACUGGGUCUC	2923	2586
AGCUACAUCUGGCUACUGGGUC	2456	2678
AGCUACAUCUGGCUACUGGG-	1393	1455
AGCUACAUCUGGCUACUGGGUCUCU	1164	1207
AGCUACAUCUGGCUACUG---	1154	1094
AGCUACAUCUGGCUACUGGGU	995	1255
AGCUACAUCUGGCUACUGG--	949	1047
AGCUACAUCUGGCUACUGGAUCU	604	965
AGCUACAUCUGGCUACUGGGCCU	514	963

hsa-miR-224-5p, chrX:151127103-151127123[-]	Normoxic	Hypoxic
CAAGUCACUAGUGGUUCCGUUUAG	313	384
CAAGUCACUAGUGGUUCCGUUU	150	329
CAAGUCACUAGUGGUUCCGUUUA	56	95
CAAGUCACUAGUGGUUCCGU-	51	70
CAAGUCACUAGUGGUUCCG--	37	43
CAAGUCACUAGUGGUUCCGUU	26	29
CAAGUCACUAGUGGUUCC---	23	25

hsa-miR-376b, chr14:101506834-101506855[+]	Normoxic	Hypoxic
AUCAUAGAGGAAAAUCCAUGU-	855	929
AUCAUAGAGGAAAAUCCAUG--	133	137
AUCAUAGAGGAAAAUCC-----	115	95
AUCAUAGAGGAAAAUCCAUGUU	114	92
AUCAUAGAGGAAAAUCGAUGUU	86	82
-UCAUAGAGGAAAAUCCAUGU-	51	54
AUCAUAGAGGAAAAUCCA----	45	28
AUCAUAGAGGAAAAUCAAUGUU	43	25
AUCAUAGAGGAAAAUCCAU---	41	32
AUCAUAGAGGAAAAUCUAUGUU	41	31

hsa-miR-378-3p, chr5:14112430-14911245[+]	Normoxic	Hypoxic
ACUGGACUUGGAGUCAGAAGGC	275	286
ACUGGACUUGGAGUCAGAAGG	122	139
ACUGGACUUGGAGUCAAAAGGC	54	48
ACUGGACUUGGAGUCACAAGGC	37	27

hsa-miR-494, chr14:101496018-101496039[+]	Normoxic	Hypoxic
UGAAACAUACACGGGAAACCUCU	1521	2220
UGAAACAUACACGGGAAACCACU	410	570
UGAAACAUACACGGGAAGCCUCU	234	266
UGAAACAUACACGGGAAACC--	220	288
UGAAACAUACACGGGAAACCUC	218	271
UGAAACAUACACGGGAAACCUCUU	190	293
UGAAACAUACACGGGAAUCCUCU	186	229
UGAAACAUACACGGGAACCCUCU	128	160
UGAAACAUACACGGGAAACCU-	96	136
UGAAACAUACACGGGAAACCACU	49	54

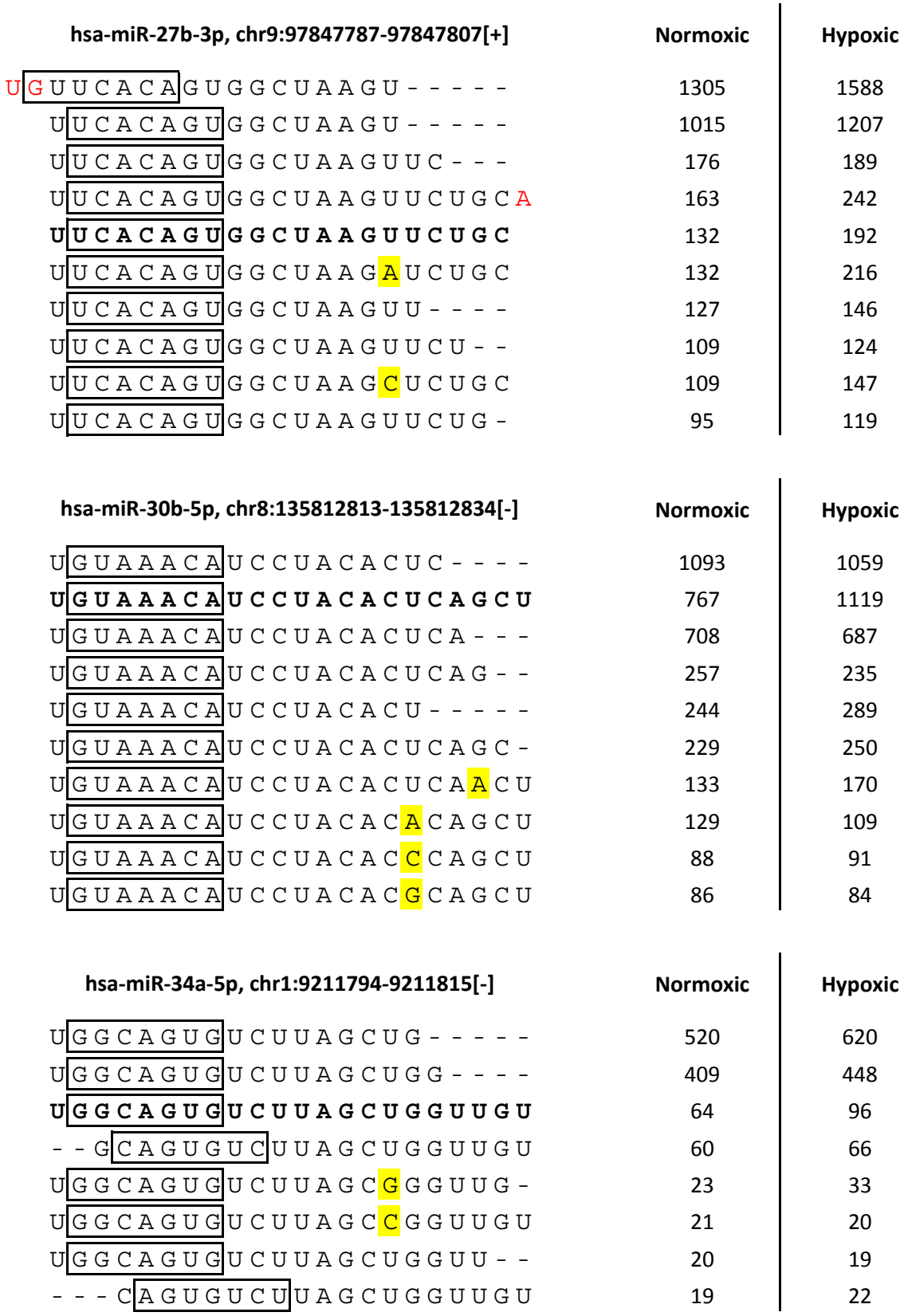
hsa-miR-6715p, chr7:150935535-150935557[+]	Normoxic	Hypoxic
AGGAAGCCCUGGAGGGGCUGGAGG	283	277
AGGAAGCCCUGGAGGGGCUGGA-	156	141
AGGAAGCCCUGGAGGGGCUGGAG	125	152
AGGAAGCCCUGGAGGGGCGGGAGG	60	48
AGGAAGCCCUGGAGGGGCUGG--	52	45
AGGAAGCCCUGGAGGGGCCGGAG	46	45
AGGAAGCCCUGGAGGGGCCGGAGG	41	41
AGGAAGCCCUGGAGGGGCGGGAG	29	41
-GGAAGCCCUGGAGGGGCUGGAGG	29	36
----AGCCCUGGAGGGGCUGGAGGU	20	22

Figure S5 B

hsa-let-7c, chr21:17912158-17912179[+]	Normoxic	Hypoxic
UGAGGUAGUAGGUUGUA-----	1900	2792
UGAGGUAGUAGGUUGUAUGGUU	1477	2456
UGAGGUAGUAGGUUGUAUGG--	732	1093
UGAGGUAGUAGGUUGUAU----	723	1078
UGAGGUAGUAGGUUGUCUGGUU	422	729
UGAGGUAGUAGGUUGUAUG---	352	471
UGAGGUAGUAGGUUGUAUGGU-	239	346
UGAGGUAGUAGGUUGUAGGGUU	224	352
UGAGGUAGUAGGUUGUAUCGUU	219	297
UGAGGUAGUAGGUUGUACGGUU	205	321

hsa-miR-15b-5p, chr3:160122395-160122416[+]	Normoxic	Hypoxic
UAGCAGCACAUCAUGGUUUAC-	232	195
-AGCAGCACAUCAUGGUUUAC-	122	76
UAGCAGCACAUCAUGGU-----	111	51
UAGCAGCACAUCAUGGUUUACA	89	63
--GCAGCACAUCAUGGGUUACA	83	67
UAGCAGCACAUCAUGGUU----	63	29
--GCAGCACAUCAUGGUUUACA	58	46
--GCAGCACAUCAUGGUUUAC-	39	29
---CAGCACAUCAUGGUUUACA	21	25
---CAGCACAUCAUGGUUUAC-	16	21

hsa-miR-16-5p, chr3:160122542-160122563[+], chr13:50623163-50623184[-]	Normoxic	Hypoxic
UAGCAGCACGUAAAUAU-----	755	506
UAGCAGCACGUAAAUAUUGGC-	238	158
UAGCAGCACGUAAAUAUUGG--	192	136
UAGCAGCACGUAAAUAUAGGCG	167	132
UAGCAGCACGUAAAUAUGGGCG	129	88
UAGCAGCACGUAAAUAUUG---	67	32
UAGCAGCACGUAAAUAUAGGC-	61	46
UAGCAGCACGUAAAUAUUGGCG	55	26
UAGCAGCACGUAAAUAUCGG--	52	35
---CAGCACGUAAAUAUUGGC-	43	25


hsa-miR-27b-3p, chr9:97847787-97847807[+]
Normoxic
Hypoxic
UGUUCACAGUGGCUAAGU-----
1305
1588
UUCACAGUGGCUAAGU-----
1015
1207
UUCACAGUGGCUAAGUUC---
176
189
UUCACAGUGGCUAAGUUCUGCA
163
242
UUCACAGUGGCUAAGUUCUGC
132
192
UUCACAGUGGCUAAGAUCUGC
132
216
UUCACAGUGGCUAAGUU----
127
146
UUCACAGUGGCUAAGUUCU--
109
124
UUCACAGUGGCUAAGCUCUGC
109
147
UUCACAGUGGCUAAGUUCUG-
95
119
hsa-miR-30b-5p, chr8:135812813-135812834[-]
Normoxic
Hypoxic
UGUAAACAUCCUACACUC----
1093
1059
UGUAAACAUCCUACACUCAGCU
767
1119
UGUAAACAUCCUACACUCA---
708
687
UGUAAACAUCCUACACUCAG--
257
235
UGUAAACAUCCUACACU-----
244
289
UGUAAACAUCCUACACUCAGC-
229
250
UGUAAACAUCCUACACUCAACU
133
170
UGUAAACAUCCUACACACAGCU
129
109
UGUAAACAUCCUACACCCAGCU
88
91
UGUAAACAUCCUACACGCAGCU
86
84
hsa-miR-34a-5p, chr1:9211794-9211815[-]
Normoxic
Hypoxic
UGGCAGUGUCUUAGCUG-----
520
620
UGGCAGUGUCUUAGCUGG----
409
448
UGGCAGUGUCUUAGCUGGUUGU
64
96
--GCAGUGUCUUAGCUGGUUGU
60
66
UGGCAGUGUCUUAGCGGGUUG-
23
33
UGGCAGUGUCUUAGCCGGUUGU
21
20
UGGCAGUGUCUUAGCUGGUU--
20
19
---CAGUGUCUUAGCUGGUUGU
19
22

hsa-miR-126-5p, chr9:139565068-139565088[+]	Normoxic	Hypoxic
CAUUAUUACUUUUGGGACGCG	1511	1576
CAUUAUUACUUUUGGUACGCG	742	874
CAUUAUUACUUUUGGAACGCG	398	329
-AUUAUUACUUUUGGGACGCG	359	482
CAUUAUUACUUUUGGUACGC-	258	286
CAUUAUUACUUUUGGUAC---	230	232
-AUUAUUACUUUUGGUACGCG	201	271
CAUUAUUACUUUUGGUACACG	202	223
CAUUAUUACUUUUGGUA----	183	208
CAUUAUUACUUUUGGUACG--	168	228

hsa-miR-151-5p, chr8:141742722-141742742[-]	Normoxic	Hypoxic
UCGAGGAGCUCACAGUCUAGUC	1355	1746
UCGAGGAGCUCACAGUCUAGU	911	1371
UCGAGGAGCUCACAGUCUAG-	668	876
UCGAGGAGCUCACAGUC----	648	755
UCGAGGAGCUCACAGGCUAGU	441	686
UCGAGGAGCUCACAGUCU---	371	425
UCGAGGAGCUCACAGUCUA--	141	180
UCGAGGAGCUCACAGUCCAGUC	80	99
UCGAGGAGCUCACAGUCCAGU	68	92
--GAGGAGCUCACAGGCUAGU	31	73

hsa-miR-199a-5p, chr1:172113732-172113754[-], chr19:10928145-10928167[-]	Normoxic	Hypoxic
CCCAGUGUUCAGACUACCUGUU-	252	220
CCCAGUGUUCAGACUACCUGU--	130	99
CCCAGUGUUCAGACUACCUGUUC	111	54
CCCAGUGUUCAGACUACCUG---	92	81
CCCAGUGUUCAGACUACC-----	47	31

hsa-miR-455-3p, chr9:116971767-116971787[+]	Normoxic	Hypoxic
AUGCAGUCCAUGGGCAUAUACAC	238	198
GCAGUCCAUGGGCAUAUACAC	220	261
UGCAGUCCAUGGGCAUAUACAC	66	56

hsa-miR-574-3p, chr4:38869713-38869734[+]	Normoxic	Hypoxic
CACGCUCAUGCACACACCCAC-	1026	1541
CACGCUCAUGCACACACCCACA	751	1445
CACGCUCAUGCACACACCCA--	101	129
CACGCUCAUGCACACACGCCACA	84	103
CACGCUCAUGCACACACCC---	81	108
CACGCUCAUGCACACACACCACA	80	148
CACGCUCAUGCACACACUCCACA	75	108
CACGCUCAUGCACACACGCCACA	68	105
CACGCUCAUGCACACCUCCCAC-	55	67
CACGCUCAUGCACACACC----	36	72

hsa-miR-744-5p, chr17:11985226-11985247[+]	Normoxic	Hypoxic
UGCGGGGCUAGGGCUAACAGC-	116	126
UGCGGGGCUAGGGCUAACAGCA	96	119
UGCGGGGCUAGGGCUAACAG--	49	54
UGCGGGGCUAGGGCUAGCAGCA	36	36
UGCGGGGCUAGGGCUACCAGCA	30	28
UGCGGGGCUAGGGCUAAC----	27	24
UGCGGGGCUAGGGCUAACA---	26	29
UGCGGGGCUAGGGCUAUCAGCA	21	27
UGCGGGGCUAGGGCUAACACA	21	24

hsa-miR-18b-5p, chrX:133304114-133304136[-]	Normoxic	Hypoxic
UAAGGUGCAUCUAGUGC------	297	253
UAAGGUGCAUCUAGUGCA-----	190	130
UAAGGUGCAUCUAGUGCAG----	105	92
UAAGGUGCAUCUAGUGCAGCUAG	72	45
UAAGGUGCAUCUAGUGCAGGUAG	58	43
UAAGGUGCAUCUAGUGCAGU---	39	26
-AAGGUGCAUCUAGUGCA-----	30	25
UAAGGUGCAUCUAGUGCAGUUAG	26	15

hsa-miR-23b-3p, chr9:97847547-97847567[+]	Normoxic	Hypoxic
AUCACAUUGCCAGGGAU----	3150	2946
AUCACAUUGCCAGGGAUU---	2875	3264
AUCACAUUGCCAGGGAUUACCA	2386	2694
AUCACAUUGCCAGGGAUUACCAC	1698	2523
AUCACAUUGCCAGGGAUUACC	1651	2226
AUCACAUUGCCAGGGAUUCCC	1085	1326
AUCACAUUGCCAGGGAUUCCCA	1042	1202
AUCACAUUGCCAGGGAUUAC-	464	622
AUCACAUUGCCAGGGAUUA--	386	438
AUCACAUUGCCAGGGAUUGCCA	319	308

hsa-miR-320c, chr18:19263520-19263539[+], chr18:21901680-21901699[+]	Normoxic	Hypoxic
AAAAGCUGGGUUGAGAG---	1573	2234
AAAAGCUGGGUUGAGAGG--	1033	1360
-AAAGCUGGGUUGAGAGG--	130	194
AAAAGCUGGGUUGAGAGGG-	58	63
AAAAGCUGGGUUGAGAGGGU	33	40

hsa-miR-365-3p, chr16:14403197-14403218[+], chr17:29902497-29902518[+]	Normoxic	Hypoxic
UAAUGCCCCUAAAAAUCCUUAU	147	187
UAAUGCCCCUAAAAAUCCUUAU	96	133
-AAUGCCCCUAAAAAUCCUUAU	90	90
UAAUGCCCCUAAAAAUCCUUAU	53	46
-AAUGCCCCUAAAAAUCCUUAU	33	37

hsa-miR-505-3p, chrX:139006319-139006340[-]	Normoxic	Hypoxic
-GUCAACACUUGCUGGUUUCCU	333	518
-GUCAACACUUGCUGGUUUCC-	142	216
CGUCAACACUUGCUGGUUUCCU	94	147
-GUCAACACUUGCUGGUUACCU	52	67
-GUCAACACUUGCUGGUUUC--	41	54
-GUCAACACUUGCUGGUUGCCU	39	42
-GUCAACACUUGCUGGUUCCCU	37	53
CGUCAACACUUGCUGGUUUCCU	35	48
-GUCAACACUUGCUGGUUUCCU	18	26
-GUCAACACUUGCUGGUAUCCU	16	18

Figure S6

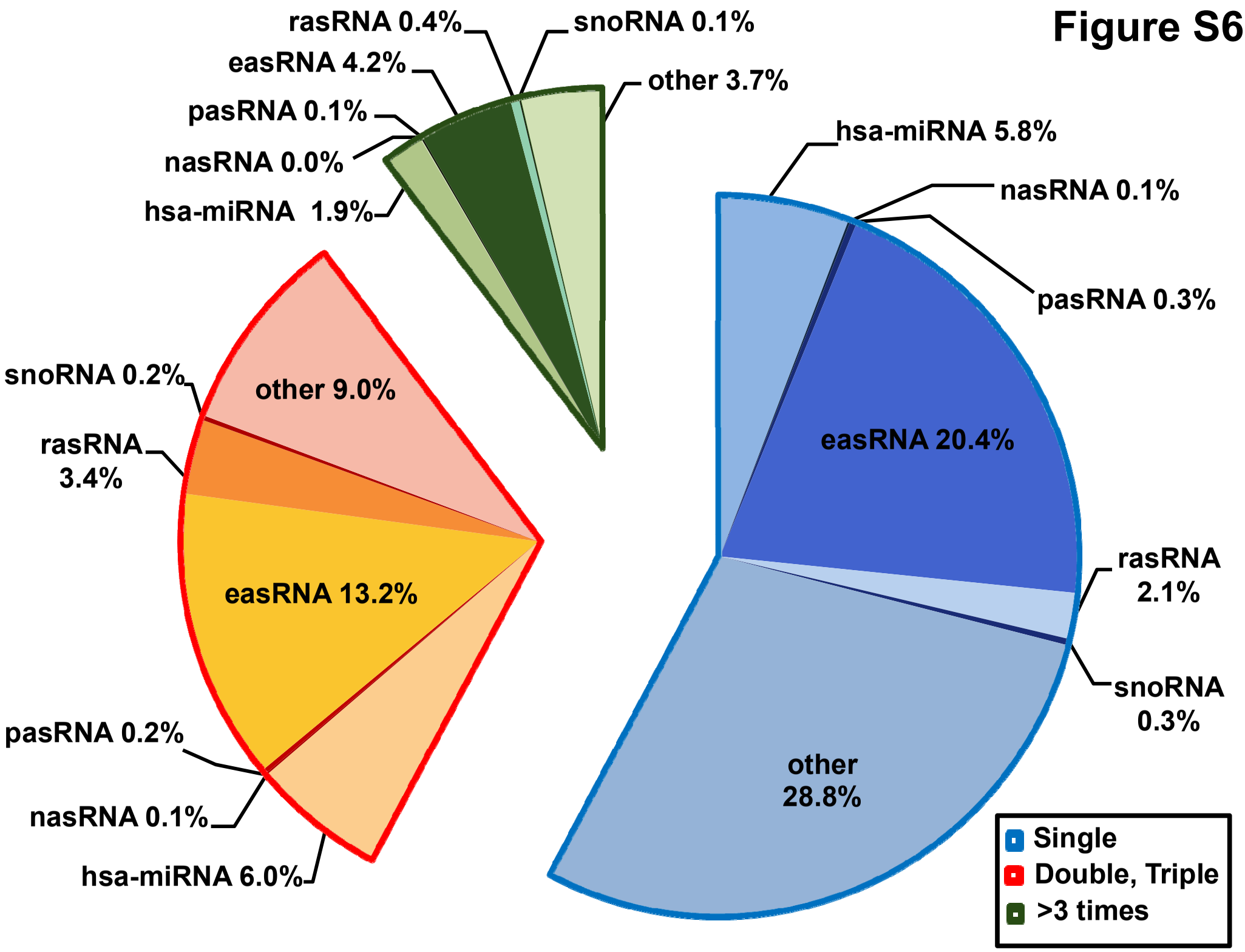
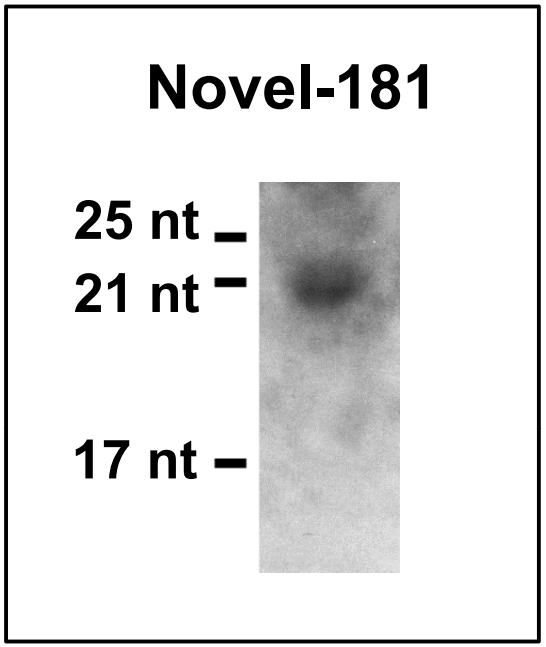

rasRNA 0.4%
snoRNA 0.1%
easRNA 4.2%
other 3.7%
pasRNA 0.1%
nasRNA 0.0%
hsa-miRNA 1.9%
hsa-miRNA 5.8%
nasRNA 0.1%
pasRNA 0.3%
snoRNA 0.2%
other 9.0%
rasRNA 3.4%
easRNA 20.4%
easRNA 13.2%
rasRNA 2.1%
snoRNA 0.3%
pasRNA 0.2%
other 28.8%
nasRNA 0.1%
hsa-miRNA 6.0%
Single
Double, Triple
>3 times

Figure S7

A



B

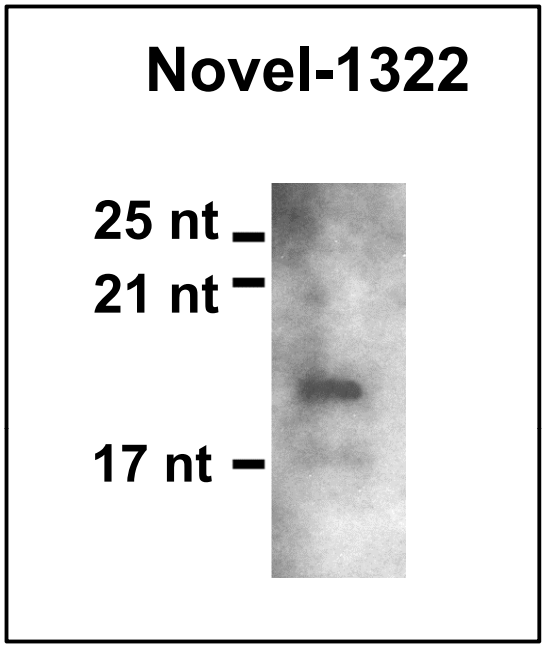


Figure S8

Novel-53

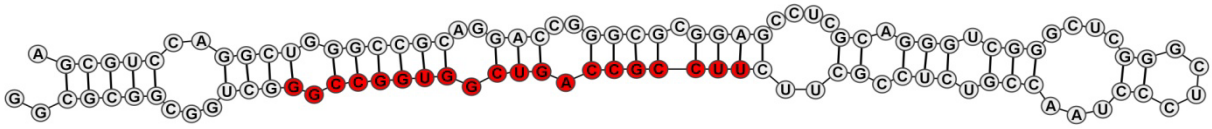
Hairpin Coordinates: chr1:20960172-20960281[+]

Mature Sequence: 78 - TTCCGCCAGTCGGTGGCCGG - 97

Context: Exonic

Free Energy: -57.1 kcal/mol

phastCons46way: Primates 0.1; mammals 0.98; vertebrates 0.99



Novel-112

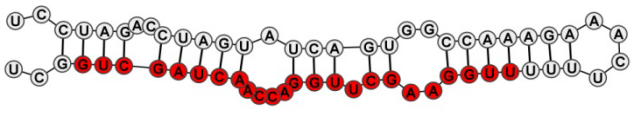
Hairpin Coordinates: chr1:44304294-44304355[+]

Mature Sequence: 36 - TTGGAAGCTTGGACCAACTAGCTG - 59

Context: Intronic

Free Energy: -33.5 kcal/mol

phastCons46way: Primates 0.89; mammals 0.05; vertebrates 0.08



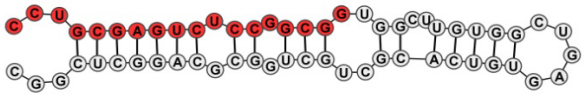
Novel-144

Hairpin Coordinates: chr1:63792596-63792655[-]

Mature Sequence: 1 - CCTGCGAGTCTCCGGCG - 16

Free Energy: -30.9 kcal/mol

phastCons46way: Primates 0.56; mammals 0.17; vertebrates 0.18



Novel-298

Hairpin Coordinates: chr10:2118213-2118283[-]

Mature Sequence: 38 - TCCTCATCACACTGCACCTTAG - 59

Context: Extragenic

Free Energy: -36.7 kcal/mol

phastCons46way: Primates 0.00; mammals 0.00; vertebrates 0.00

Novel-301

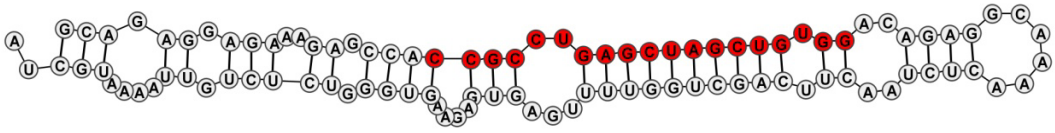
Hairpin Coordinates: chr10:4033352-4033451[+]

Mature Sequence: 19 - CCGCCTGAGCTAGCTGTGG - 37

Context: Extragenic

Free Energy: -32.2 kcal/mol

phastCons46way: Primates 0.00; mammals 0.00; vertebrates 0.00



Novel-1691

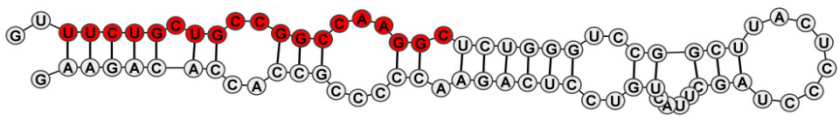
Hairpin Coordinates: chr2:86010723-86010800[-]

Mature Sequence: 3 - TTCTGCTGCCGGCCAAGGC - 21

Context: Intronic

Free Energy: -35.2 kcal/mol

phastCons46way: Primates 0.02; mammals 0.10; vertebrates 0.09



Novel-716

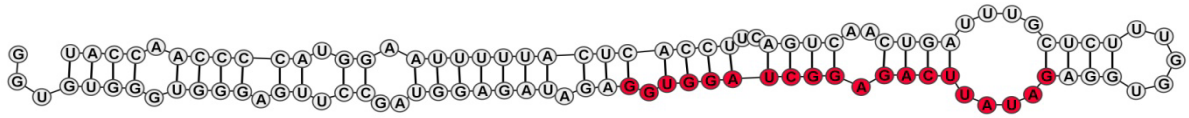
Hairpin Coordinates: chr12:66417400-66417506[-]

Mature Sequence: 58 - GATATTCAGAGGCTAGGTGG - 77

Context: Extragenic

Free Energy: -37.2 kcal/mol

phastCons46way: Primates 0.00; mammals 0.00; vertebrates 0.00



Novel-2177

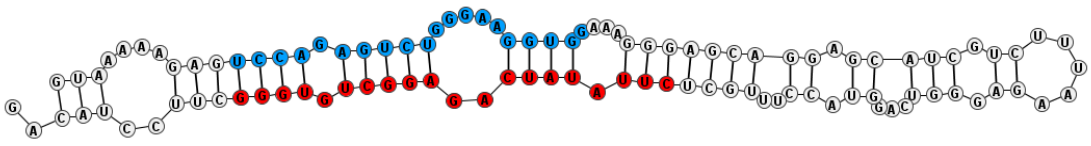
Hairpin Coordinates: chr3:124093179-124093284[+]

Mature Sequence: 77 - CTTATATCAGAGGCTGTGGG - 96

Context: Intronic

Free Energy: -33.0 kcal/mol

phastCons46way: Primates 0.11; mammals 0.00; vertebrates 0.00



Novel-869

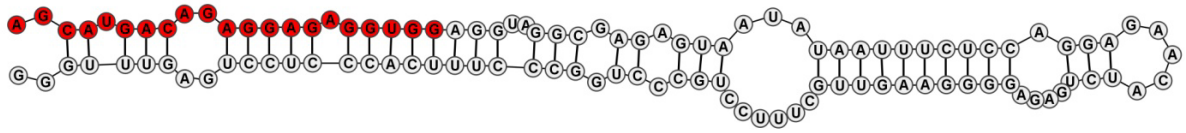
Hairpin Coordinates: chr14:50433117-50433229[+]

Mature Sequence: 1 - AGCATGACAGAGGAGAGGTGG - 21

Context: Extragenic

Free Energy: -41.6 kcal/mol

phastCons46way: Primates 0.00; mammals 0.00; vertebrates 0.00



Novel-2366

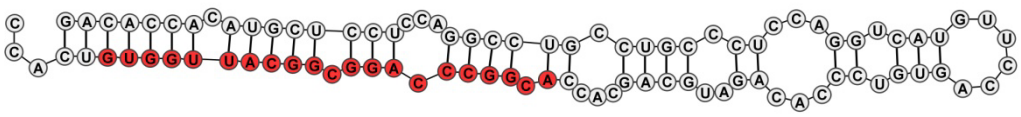
Hairpin Coordinates: chr5:1510877-1510971[-]

Mature Sequence: 70 - ACGGCCCAGGCGGCATTGGTG - 90

Context: Intronic

Free Energy: -36.9 kcal/mol

phastCons46way: Primates 0.10; mammals 0.09; vertebrates 0.10



Novel-992

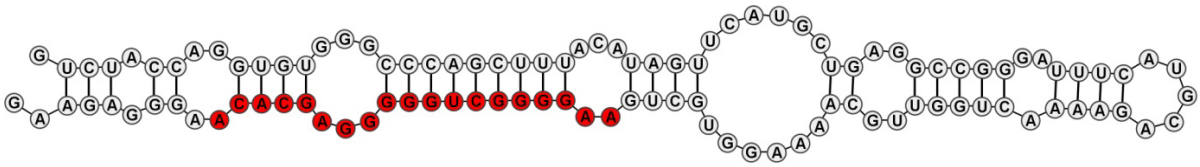
Hairpin Coordinates: chr15:62635228-62635337[+]

Mature Sequence: 84 - AAGGGGCTGGGGGAGCACA - 102

Context: Extragenic

Free Energy: -38.1 kcal/mol

phastCons46way: Primates 0.02; mammals 0.00; vertebrates 0.00



Novel-2982

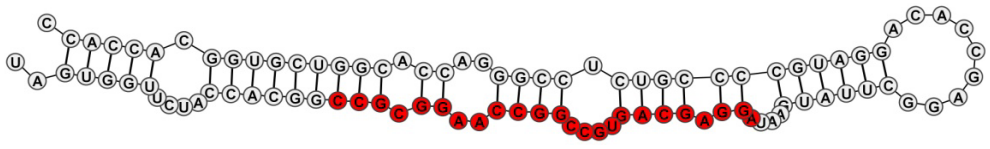
Hairpin Coordinates: chr9:97827632-97827728[+]

Mature Sequence: 57 - AGGAGCAGTGCCGGCCAAGGCGCC - 80

Context: Intronic

Free Energy: -48.0 kcal/mol

phastCons46way: Primates 0.00; mammals 0.03; vertebrates 0.03



Novel-1322

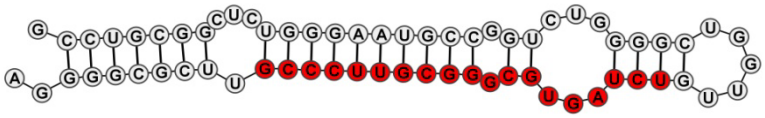
Hairpin Coordinates: chr17:62776877-62776942[+]

Mature Sequence: 38 - TCTAGTGCGGGCGTTCCCG - 56

Context: Exonic

Free Energy: -36.2 kcal/mol

phastCons46way: Primates 0.02; mammals 0.00; vertebrates 0.00



Novel-1966

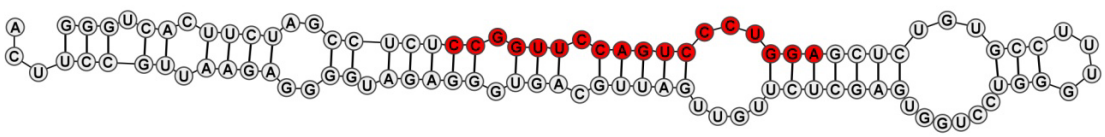
Hairpin Coordinates: chr21:45029768-45029870[-]

Mature Sequence: 19 - CCGGTTCCAGTCCCTGGAG - 37

Context: Intronic

Free Energy: -38.5 kcal/mol

phastCons46way: Primates 0.02; mammals 0.00; vertebrates 0.00



Novel-2019

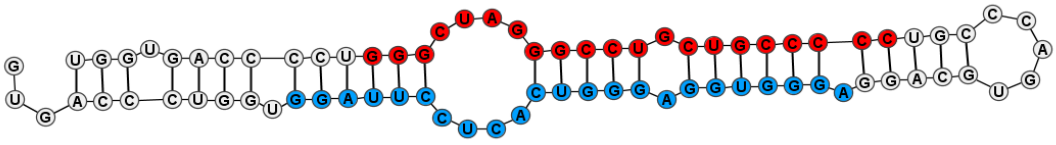
Hairpin Coordinates: chr22:35732714-35732792[-]

Mature Sequence: 12 - GGGCTAGGGCCTGCTGCCCCC - 32

Context: Intronic

Free Energy: -45.4 kcal/mol

phastCons46way: Primates 0.01; mammals 0.00; vertebrates 0.00



Novel-181

Hairpin Coordinates: Chr1: 143672921-143673002 [+]

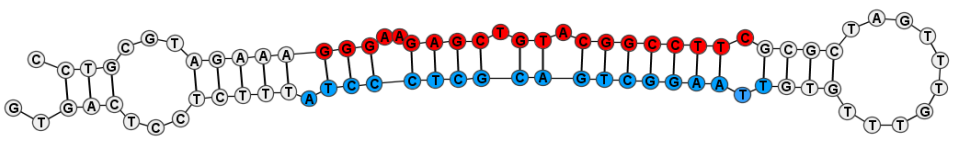
Hairpin Coordinates: Chr1: 147860434-147860515 [+]

Mature Sequence: 13 - GGGAAGAGCTGTACGGCCTTC - 33

Context: Intronic

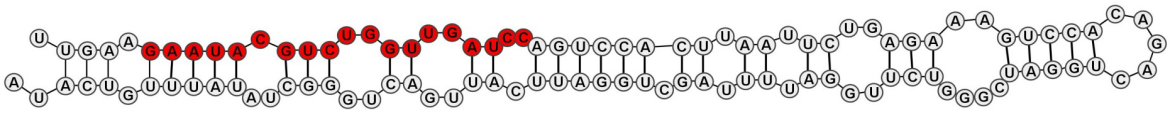
Free Energy: -30.1 kcal/mol

phastCons46way: Primates 0.01; mammals 0.01; vertebrates 0.01



Novel-2339

Hairpin Coordinates:	Chr4: 172107335- 172107443 [+]
Mature Sequence:	6 - GAATACGTCTGGTTGATCC - 24
Context:	Extragenic
Free Energy:	-33.7 kcal/mol
phastCons46way:	Primates 0.01; mammals 0.00; vertebrates 0.00



Novel-498

Hairpin Coordinates:	Chr11: 15991079- 15991167 [-]
Mature Sequence:	48 - GGTAGTGAGTTATCAGCTAC -67
Context:	Exonic
Free Energy:	-35.6 kcal/mol
phastCons46way:	Primates 0.25; mammals 0.12; vertebrates 0.67

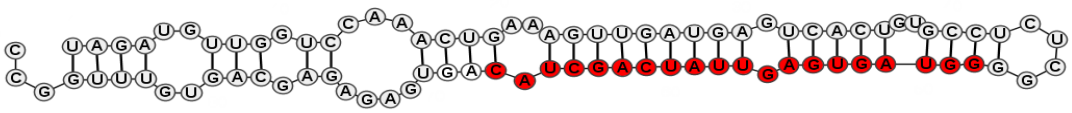


Figure S9

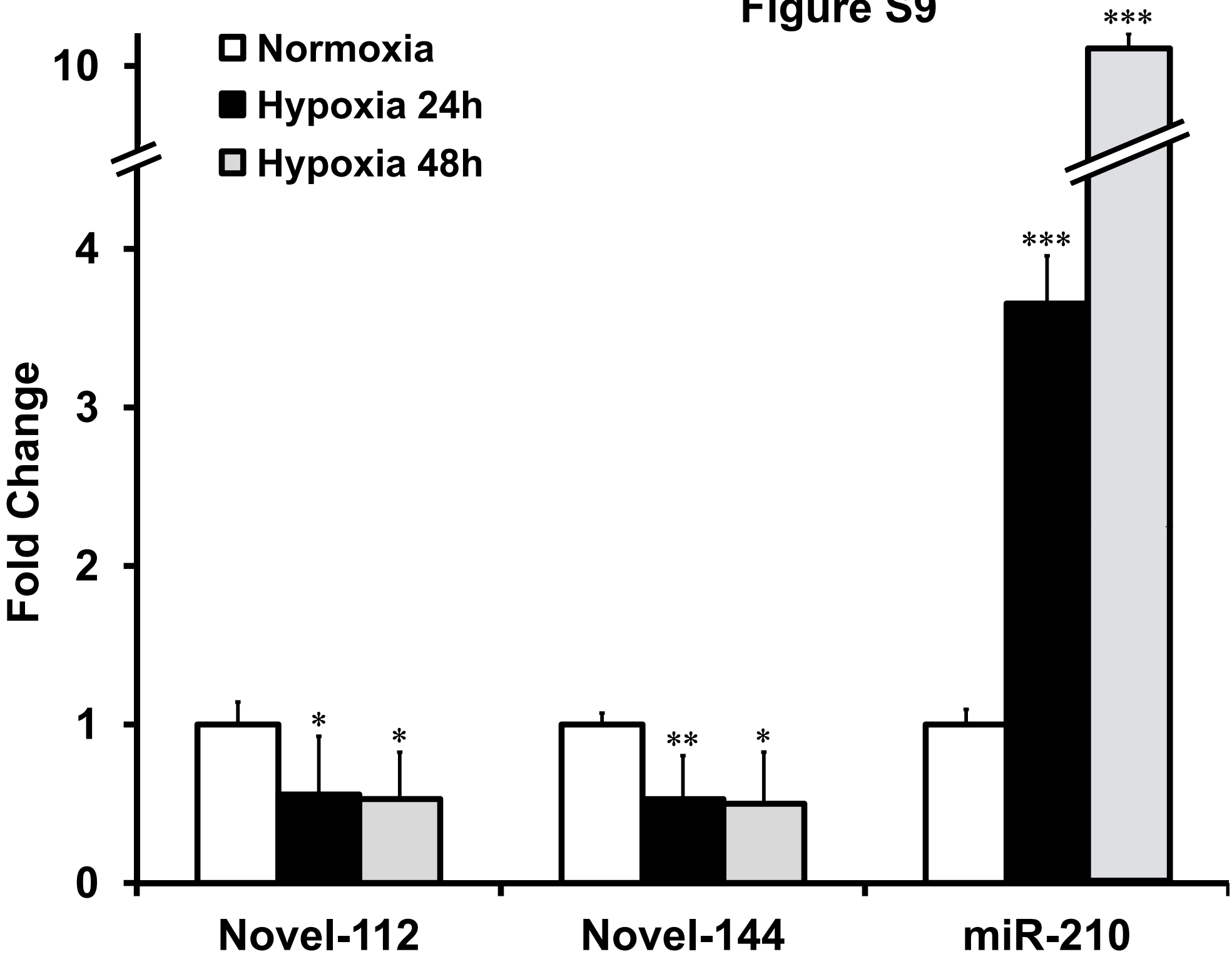

Normoxia
Hypoxia 24h
Hypoxia 48h
Fold Change
10
4
3
2
1
0
*
*
**
*
***
***
Novel-112
Novel-144
miR-210

Table S2. Characteristcs of isomiRs in endothelial cells.

	Hits	Isoforms*	miRNA-species
ALL	1,834,650	3,153	230
Exact Length & Sequence	535,589	206	206
5' and 3' variations	461,332	657	73
5' variations	638,510	1,200	106
3' variations	884,297	1,739	183
Variance in Sequence - Exact length	237,586	666	127
Variance in Sequence - 5' or 3' variations	235,608	1,258	101

* Comprises annotated and variations