

Figure S1. Conservation of sequences of (a) miR-136 (b) miR-127 (c) miR-433 (d) miR-432 and (e) miR-431. microRNAs (antisense) shown above mRNA sequences (sense); dots represent nucleotide identical to human *RTL1*. *Homo* (human, euarchontoglires), *Ovis* (sheep, laurasiatherian), *Orycteropus* (aardvark, afrotherian), *Dasypus* (armadillo, xenarthran).

Figure S2. Self-complementarity of (a) miR-127-3p and (b) miR-433-3p. Predicted hairpin structures of pre-miR-127 and pre-miR-433 were obtained from miRDB [58]. The mature microRNAs processed from pre-miRNA hairpins are indicated by yellow background. miRNA seed sequences indicated in red.

Figure S3: Alignment of seven 33-nucleotide TRB repeats for *RTL1* genes (sense strand) of diverse eutherian species. Nucleotides in red and blue are complementary to pre-miR-432. Blue sequences are complementary to the seeds of miR-432-5p and miR-432-3p (miR-432-5p target *cuccaag* occurs twice; miR-432-3p target *ccaucca* occurs once within pre-miR-432). The TRB repeats are disrupted in mouse and rat *Rtl1* genes (see Figure S4).

Figure S4: Partial sequence of the mouse *RTL1* mRNA showing 12-nucleotide TRA repeats, 66-nucleotide TRB2 repeats, and 24-nucleotide TRC repeats. The TRB2 and TRC repeats have been derived from within the ancestral 33-nucleotide TRB repeats. Sequences in blue are complementary to the seed sequences of miR-432-5p and miR-432-3p. Sequences in red are complementary to the seed sequences of miR-434-5p and miR-434-3p.

Figure S5. Autotargets and allotargets of miR-434-5p and miR-434-3p in the sequence of mouse *Rtl1* mRNA. These complex relations are a consequence of the 24-nucleotide TRC repeats.

Figure S6. (a) The pre-miR-432 hairpin: CUUGGAG is the seed of miR-432-5p (appears twice); UGGAUGG is the seed of miR-432-3p; 33-nucleotide periodicity of TRB repeats indicated by successive arrow heads. (b) The pre-miR-434 hairpin: CUCGACU (appears twice) is the seed of miR-434-5p; UUGAACC (appears thrice) is the seed of miR-434-3p; 24-nucleotide periodicity of TRC repeats is indicated by successive arrow heads. The mature microRNAs processed from the hairpins are indicated by yellow. Structures of pre-miRNA hairpins from miRdb [58].

(S1a) miR-136-3p miR-136-5p

3' -UCUGAGUAAACUCUGCUACUAC-5' 3' -AGGUAGUAGUUUUGUUUACCUC-5'

|||||

5' -UGAAGACUCAUUUGAGACGAUGAUGGAGCAUAAGAAUCCAUCAUCAAACAUAUGGAGUCCUC-3' Homo

.....G..... Ovies

.....G..... Orycteropus

.....G..G..... Dasypus

(S1b) miR-127-3p miR-127-5p

3' -UCGGUUCGAGUCUGCCUAGGCU-5' 3' -UAGUCUCGGGAGACUCGAAGUC-5'

|||||

5' -ACCAGCCAAGCUCAGACGGAUCCGAUGAUCUUUCUGAAUCAGAGCCCUCUGAGCUUCAGCAG-3' Homo

..... Ovies

..... Orycteropus

..... Dasypus

(S1c) miR-433-3p miR-433-5p

3' -UGUGGCUCUCGGGUAGUACUA-5' 3' -CUUAUUACUGUCCGAGUGGCAU-5'

|||||

5' -AGAACACCGAGGAGCCC AUCAUGAUCCUUCUCAACACAGAGGAUCUAGCCUCUCUGAAUAAUGACAGGCUCACCGUACUU-3' Homo

.....G..... Ovies

.....C..... Orycteropus

.....AGAU..... Dasypus

(S1d) miR-432-3p miR-432-5p

3' -UCUGUACCUCUCGGUAGGUC-5' 3' -GGUGGGUUACUGGAUGAGGUUCU-5'

|||||

5' -CUCCAAGACAUGGAGGAGCCAUCAGUGGCCACGUAAGGAAUAGAGGAUCCACCCAAUGACCUACUCCAAGACCU-3' Homo

.G.....A..G.....A.....U..... Ovies

.....A.C.....A..... Orycteropus

.G.....U..C.....G.A.....U..... Dasypus

(S1e) miR-431-3p miR-431-5p

3' -UCUUCGGGACGUUCUGCUGGAC-5' 3' -ACGUACUGCCGGAUGUUCUGU-5'

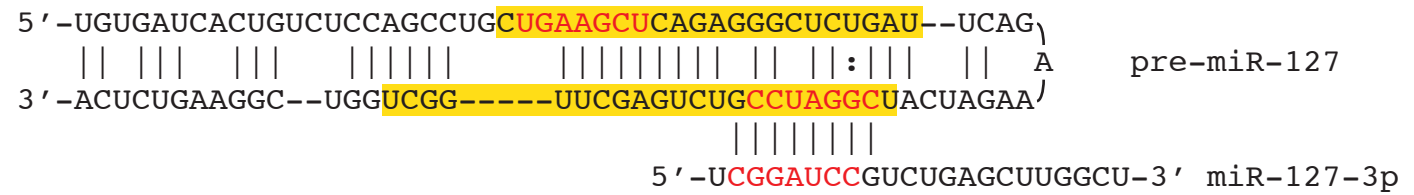
|||||

5' -GCGAGAAGCCUGCAAGACGACCUAGCAACGUUACCGUCAGUGUGGCCUGCAUGACGGCCUGCAAGACACCU-3' Homo

.....C.....U..... Ovies

.....C....G...G.G.....AG.....C..... Orycteropus

(S2a)



(S2b)

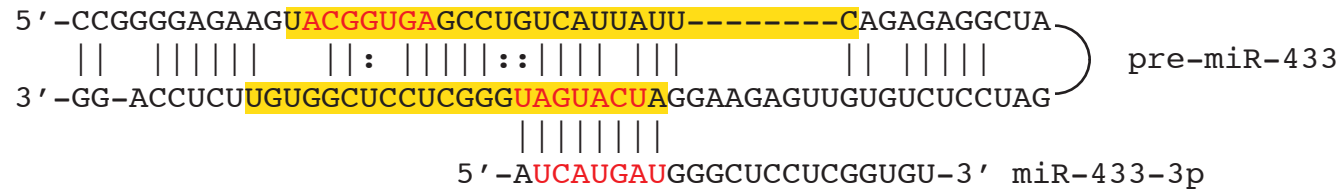


Figure S3

uggagugcggggagaggcagggccagccagcgg-Homo
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ugcagugcaggagaaggcgggaccagccaaggg-Heterocephalus
uggagcgcaggagacggaggggcccagcugaggg-Cavia
aggcgcgcaggagggggcggggcccgcgg-Oryctolagus
cgaagcacaggaggug*aggcagcggccccggc-Ochotona
cggcagagcggaggcgggcggggucggccg----Ovies
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ccaagugcaggaagcguuggagccagccagugg-Trichechus
ccgagcgcaggaagcguuggagccagccagcag-Orycteropus
ccaggcgcaggcaggg-----Dasypus

* auggcccaggcagcggccc Ochotona

cccagcccaggaaaagaaggagccccccagugg-Homo
cccagcccgggaaaaaagagagccacccagugg-Galeopterus
cccagcccaggaaaagccaggagccaccaagugg-Nannospalax
cggagcccaggaaaagcaaggagccccccagugg-Heterocephalus
cccggcgaggaaaagcaaggagcaucccagugg-Cavia
cccagcccagggaaggagagccacccagggg-Oryctolagus
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-----gcgg-Ovies
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cccaucccaggaaaagaaagagccacccagugg-Trichechus
cucagcccaggaaaaggaaggagccacccagugg-Orycteropus
----ccccaggacccccagcagccccccagcga-Dasypus

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cucacuccaggaaauggaagagcugcccacuga-Galeopterus
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cucuuccaggaaaugaagagcugccuacuga-Heterocephalus
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cccucaggaggagcuggaagagcugcccacuga-Ochotona
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ucuacuccaagacauggaggagccauccagugg-Homo
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ucuacuccaagacauggaggagccauccagugg-Heterocephalus
ucuacuccaagacauggaggagccauccagugg-Cavia
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ucuacuccaagacauggaggagccauccagugg-Orycteropus
cguccgccaagccauggaggagccauccagugg-Dasypus

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ccuacuccaagaccuggaggagucaugcaacgg-Homo
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 ccuacuccaagacuuggaggaguca---cacgu-*Dasypus*

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 uucacgccaggaaaugggggauccacgcauga-Trichechus
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Figure S4

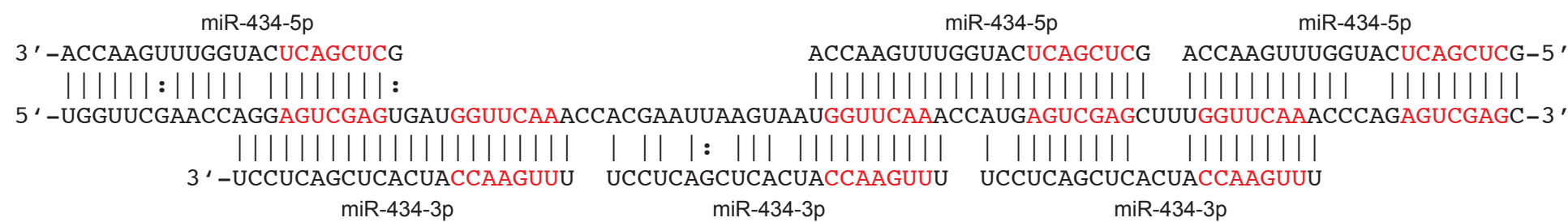
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gggcccaggcgg
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aggcccaggcgg
aggcucaggcug
aagcccagguug
aggcccagguug

TRB2 repeats
aggcccaggcggggccagccagcggcccagcccaggaaaagaaggagccccccaguggcccacuccaggaaauggaaga
gcugcccacugaucuauccaaagacauggaggagccauccaguggcccacguaaggaaaauagagga
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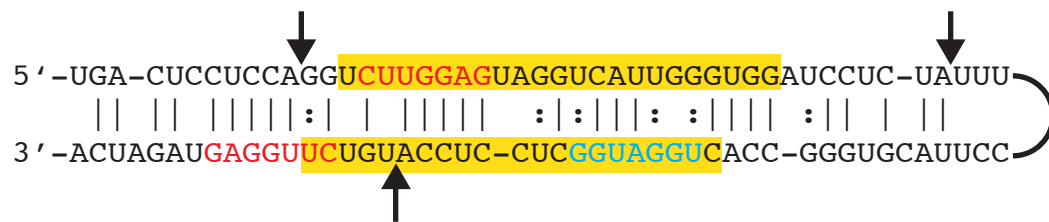
TRC repeats
agucaagugauuuucaaaaccagggaaggguucgga
accacucagugagggauccgauuauagcaugga

TRB repeats

(Figure S5)



(6a)



(6b)

