



Figure S1: Relative miRNA expression levels in (A) *Bathyergus suillus*, (B) *Cryptomys hottentotus hottentotus*, (C) *Cryptomys hottentotus mahali*, (D) *Cryptomys hottentotus pretoriae*, (E) *Georychus capensis*, and (F) *Heterocephalus glaber* brain tissue in response to hypoxia. Data are mean \pm SEM, $n = 4$ RNA isolations from different individuals for each species. Asterisks indicate data that are significantly different from the control condition ($p < 0.05$).

Table S1: MiRNA sequences and forward primers designed from *Heterocephalus glaber* (hgl).

miRNA	Mature sequence (5' - 3')	Primer (5' - 3')
hgl-let-7f-5p	UGAGGUAGUAGAUUGUAUAGUU	ACACTCCAGCTGGGTGAGGTAGTAGATTG
hgl-miR-17-3p	ACUGCAGUGAGGGGCACUUGUAG	ACACTCCAGCTGGGCTGCAGTGAGGGCAC
hgl-miR-24-5p	UGCCUACUGAGCUGAUAUACAGU	ACACTCCAGCTGGGTGCCTACTGAGCTGA
hgl-miR-24-3p	GGCUCAGUUCAGCAGGAACAG	ACACTCCAGCTGGGGGCTCAGTTCAGCAG
hgl-miR-26b-5p	UUCAAGUAAUUCAGGAUAGGU	ACACTCCAGCTGGGTTCAAGTAATTCAGG
hgl-miR-27a-5p	AGGGCUUAGCUGCUUGUGAGCA	ACACTCCAGCTGGGAGGGCTTAGCTGCTT
hgl-miR-27a-3p	UUCACAGUGGCUAAGUUCGCG	ACACTCCAGCTGGGTTACAGTGGCTAAG
hgl-miR-124-3p	UAAGGCACGCGGUGAAUGCC	ACACTCCAGCTGGGTAAGGCACGCGGTGA
hgl-miR-125b-5p	UCCUGAGACCCUAACUUGUGA	ACACTCCAGCTGGGTCCCTGAGACCCTAA
hgl-miR-126a-5p	CAUUAUUACUUUUGGUACGCG	ACACTCCAGCTGGGCATTATTACTTTTGG
hgl-miR-140-5p	CAGUGGUUUUACCCUAUGGUAG	ACACTCCAGCTGGGTGGTTTTACCCTATG
hgl-miR-140-3p	UACCACAGGGUAGAACCACGG	ACACTCCAGCTGGGACCACAGGGAAGAAC
hgl-miR-146a-5p	UGAGAACUGAAUCCAUGGGUU	ACACTCCAGCTGGGTGAGAAGTGAATTCC
hgl-miR-146a-3p	CCUGUGAAAUUCAGUUCUUCAG	ACACTCCAGCTGGGCCTGTGAAATTCAGT
hgl-miR-147-3p	GUGUGCGGAAUAGCUUCUGCUA	ACACTCCAGCTGGGGTGTGCGGAAGTGCT
hgl-miR-150-5p	UCUCCCAACCCUUGUACCAGUG	ACACTCCAGCTGGGTCTCCCAACCCCTGT
hgl-miR-199a-3p	ACAGUAGUCUGCACAUUGGUUA	ACACTCCAGCTGGGACAGTAGTCTGCACA
hgl-miR-207	GCUUCUCCUGGCUUCCUCCUC	ACACTCCAGCTGGGTCTCCTGTCTCTCCT
hgl-miR-210-5p	AGCCACUGCCCACCGCACACUG	ACACTCCAGCTGGGCCACTGCCACCGCA
hgl-miR-210-3p	CUGUGCGUGUGACAGCGGCUGA	ACACTCCAGCTGGGCTGTGCGTGTGACAG
hgl-miR-325-3p	UUUAUUGAGCACCUCUAUCAA	ACACTCCAGCTGGGTTTATTGAGCACCTA
hgl-miR-325-5p	CCUAGUAGGUGCUCAGUAAGUGU	ACACTCCAGCTGGGTAGTAGGTGCTCAGT
hgl-miR-376a-3p	AUCGUAGAGGAAAUCCACGU	ACACTCCAGCTGGGATCGTAGAGGAAAAT
hgl-miR-378-3p	ACUGGACUUGGAGUCAGAAGG	ACACTCCAGCTGGGACTGGACTTGGAGTC
hgl-miR-378-5p	CUCCUGACUCCAGGUCCUGUGU	ACACTCCAGCTGGGCTCCTGACTCCAGGT
hgl-miR-592-3p	UCAUCACGUGGUGACGCAACAU	ACACTCCAGCTGGGATCACGTGGTGACGC
hgl-miR-592-5p	AUUGUGUCAAU AUGCGAUGAUGU	ACACTCCAGCTGGGATTGTGTCAATATGC

Table S2: List of top 5 contributing factors to PC1 and PC2 for each species using the data from control and hypoxic animals and then considering all species together using only the data from hypoxic groups. Variables that are not bolded were repeats of the variables used for PCA plots (bolded). For *C. h. pretoriae*, there were only three variables that appeared above the reference line of the barplots generated by the `fviz_contrib` function, indicating only three variables contribute to PC2 in this species.

<i>Species</i>	<i>Top 5 variables contributing to PC1</i>	<i>Top 5 variables contributing to PC2</i>
<i>B. suillus</i>	26b-5p, 124-3p let-7f-5p, 378-3p, 210-3p	210-3p, 26b-5p, 24-5p, 125b-5p, 378-3p
<i>C. h. hottentotus</i>	HIF1 protein, 125b-5p, 378-3p, 27a-5p, let-7f-5p	AO capacity, 378-5p, 124-3p, 325-5p, 378-3p
<i>C. h. mahali</i>	HIF1 protein, 126a-5p, 147-3p, 27a-3p, 207	147-3p, HIF1 protein, 17-3p, 125-5p, 126a-5p
<i>C. h. pretoriae</i>	124-3p, 26b-5p, 378-3p, 150-5p, let-7f-5p	125b-5p, 26b-5p, 17-3p
<i>G. capensis</i>	147-3p, 125b-5p, 378-3p, 26b-5p, 210-3p	124-3p, 378-3p, 592-3p, 147-3p, let-7f-5p
<i>H. glaber</i>	24-3p, 27a-3p, 199a-3p, 24-5p, 150-5p	17-3p, 199a-3p, HIF1 protein, 27a-3p, let-7f
All species	26b-5p, 124-3p let-7f-5p, 378-3p, 210-3p	210-3p, 24-5p, 26b-5p, 125b-5p, 378-3p

Table S3: General functions of miRNAs implicated in the response to hypoxia in the brains of several species of mole-rats.

miRNA	Function	Reference(s)
Apoptosis		
miR-24	Inhibit apoptosis and HIF degradation	(Roscigno et al., 2017; Sun et al., 2016)
miR-27	Inhibit apoptosis	(Chen et al., 2014; Sabirzhanov et al., 2014)
miR-26 (decrease)	Anti-apoptosis, anti-autophagy	(Nallamshetty et al., 2013)
miR-147	Inhibit apoptosis	(Han et al., 2017)
miR-207	Anti-apoptosis, anti-autophagy	(Tao et al., 2015)
miR-210	Anti-apoptosis, pro-angiogenesis and tissue repair	(Meng et al., 2018; Zeng et al., 2011)
	Inhibit HIF degradation	(Bavelloni et al., 2017)
miR-378	Inhibit apoptosis	(Fang et al., 2012)
miR-592	Inhibit apoptosis Cell proliferation, Cellular metabolism	(Irmady et al., 2014) (He et al., 2018) (Haque et al., 2016; Jia et al., 2016)
	Inhibits astroglial differentiation and cell maturation	(Zhang et al., 2013)
Inflammation		
miR-124	Inhibit neuroinflammation Suppresses autophagy	(Huang et al., 2018) (Gu et al., 2016)
miR-125b	Pro-inflammatory Neuroprotective – promote neuronal lipid membranes Promotes neuronal differentiation	(Mar-Aguilar et al., 2013; Rink and Khanna, 2011; Zhang et al., 2017) (Zhang et al., 2019) (Xiu et al., 2018)
miR-140	Enhance cerebral protection	(Han et al., 2018; Truettner et al., 2013)
miR-146	5p isomer inhibits inflammation via NFκB 3p isomir increases pro-inflammatory IL-8	(Li et al., 2017; Nallamshetty et al., 2013) (Gysler et al., 2016)
miR-150	Inhibit cell proliferation and migration during stress via HIF and regulates inflammation	(Truettner et al., 2013)
miR-210	Anti-inflammatory via targeting NFκB	(Li et al., 2017)
Circadian Rhythms		
miR-325	Circadian rhythm – melatonin synthesis	(Yang et al., 2017)
Angiogenesis		
miR-let-7f	Inhibits angiogenesis through Raf-ERK	(Yao et al., 2017)
miR-126	Inhibits angiogenesis Involved in vascular integrity and cell function	(Mishra et al., 2009)
miR-199	Inhibits angiogenesis through HIF-1/VEGF	(Dai et al., 2015)

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