

Supplementary Table 2: List of differentially expressed MiRs with the number of targets in the signature(s) for the subgroup(s) in which they are differentially expressed. For each miR is listed the subgroup in which the miR was differentially expressed, the direction of the miR expression, the direction of the target gene expression, number of target miRs in the signature, hypergeometric p-value with Bonferroni adjustment, observed/expected ratio and the minimum number of databases supporting miR target prediction for the analysis. *Abbreviations.* ICUAW = ICU-acquired weakness; DBs = databases; Exp = experimentally validated database (Tarbase); 7D = Day 7 post-ICU (vs. healthy individuals); 6M = Month 6 post-ICU (vs. healthy individuals); Improver= Patient phenotype at month 6 post-ICU with increase in quadriceps cross sectional area to “normal” (sex and age matched population based norms, and > 10cm²) compared with non-improvers (sustained quadriceps wasting, increase in cross sectional area <10 cm²).

miR	Subgroup	Direction of miR expression	Direction of Target genes expression	Number of targets	Bonferroni adjusted p-value	Observed/Expected	Number of DBs predicting target interaction
hsa-miR-1321	7D	up	down	4	1.87E-01	1.78	4
hsa-miR-206	7D	down	up	62	1.45E-01	1.15	2
hsa-miR-23a-3p	7D	down	up	124	3.05E-06	1.50	Exp
hsa-miR-29a-3p	7D	down	down	72	8.19E-02	1.18	2
hsa-miR-29a-3p	7D	down	down	10	1.04E-01	1.58	4
hsa-miR-29a-3p	7D	down	up	88	4.82E-02	1.19	Exp
hsa-miR-29b-3p	7D	down	down	71	9.88E-02	1.17	2
hsa-miR-29b-3p	7D	down	down	9	1.76E-01	1.44	4
hsa-miR-29b-3p	7D	down	up	71	1.42E-01	1.14	Exp
hsa-miR-3133	7D	up	up	33	8.74E-02	1.28	3
hsa-miR-3136-3p	7D	up	up	40	8.80E-02	1.25	2
hsa-miR-3175	7D	down	up	3	9.14E-02	2.79	Exp
hsa-miR-3175	7D	down	down	3	1.44E-01	2.27	Exp
hsa-miR-3622a-3p	7D	up	down	54	1.33E-01	1.17	2
hsa-miR-3622a-3p	7D	up	down	13	1.07E-02	2.06	3
hsa-miR-424-3p	7D	down	up	11	1.94E-01	1.35	Exp
hsa-miR-424-5p	7D	down	down	51	4.66E-02	1.27	3
hsa-miR-424-5p	7D	down	up	143	1.70E-02	1.18	Exp
hsa-miR-424-5p	7D	down	down	170	3.02E-02	1.15	Exp
hsa-miR-4488	7D	down	up	4	1.03E-04	13.93	Exp
hsa-miR-4516	7D	down	up	16	9.61E-02	1.43	3
hsa-miR-4707-5p	7D	down	up	7	5.47E-02	2.05	2
hsa-miR-4707-5p	7D	down	up	2	7.72E-02	4.29	3
hsa-miR-4764-3p	7D	up	down	5	1.31E-01	1.86	3
hsa-miR-4780	7D	down	up	6	1.05E-01	1.86	3
hsa-miR-4795-5p	7D	up	up	7	1.01E-01	1.77	3
hsa-miR-502-3p	7D	down	down	12	1.95E-01	1.33	3
hsa-miR-502-3p	7D	down	down	7	2.05E-02	2.52	4
hsa-miR-502-3p	7D	down	up	26	5.28E-02	1.40	Exp
hsa-miR-548as-3p	7D	up	up	97	7.56E-02	1.15	2
hsa-miR-551a	7D	up	down	2	4.55E-02	5.67	Exp
hsa-miR-5704	7D	up	up	24	2.99E-02	1.51	2
hsa-miR-574-3p	7D	up	up	1	1.67E-01	5.57	4
hsa-miR-600	7D	up	up	20	1.17E-02	1.75	3
hsa-miR-600	7D	up	up	8	1.46E-02	2.50	4
hsa-miR-638	7D	down	up	5	8.37E-02	2.14	Exp
hsa-miR-638	7D	down	down	6	6.62E-02	2.09	Exp
hsa-miR-663a	7D	down	down	4	1.69E-01	1.85	3
hsa-miR-424-3p	6M	down	up	4	8.79E-02	2.38	3
hsa-miR-5007-3p	6M	up	up	21	1.49E-01	1.28	2
hsa-miR-181a-5p	Improver	down	up	57	1.35E-01	1.16	2
hsa-miR-181a-5p	Improver	down	down	38	1.04E-01	1.24	2
hsa-miR-181a-5p	Improver	down	up	185	1.49E-09	1.53	Exp
hsa-miR-181a-5p	Improver	down	down	132	7.93E-11	1.75	Exp
hsa-miR-196b-5p	Improver	down	down	30	3.21E-02	1.43	2
hsa-miR-196b-5p	Improver	down	up	14	1.49E-01	1.37	3
hsa-miR-196b-5p	Improver	down	down	12	2.84E-02	1.87	3
hsa-miR-196b-5p	Improver	down	up	4	1.76E-01	1.82	4
hsa-miR-196b-5p	Improver	down	down	3	1.58E-01	2.18	4
hsa-miR-196b-5p	Improver	down	up	51	5.90E-02	1.25	Exp
hsa-miR-196b-5p	Improver	down	down	42	1.13E-03	1.65	Exp
hsa-miR-205-3p	Improver	up	down	90	7.99E-02	1.16	2
hsa-miR-205-3p	Improver	up	down	30	9.69E-03	1.58	3
hsa-miR-3124-3p	Improver	up	down	31	5.11E-02	1.36	2
hsa-miR-33b-5p	Improver	down	down	42	9.21E-03	1.46	2
hsa-miR-33b-5p	Improver	down	down	16	1.52E-02	1.83	3
hsa-miR-33b-5p	Improver	down	up	7	5.98E-02	2.01	4
hsa-miR-33b-5p	Improver	down	down	5	6.75E-02	2.29	4
hsa-miR-33b-5p	Improver	down	up	38	5.23E-05	1.98	Exp
hsa-miR-33b-5p	Improver	down	down	18	5.80E-02	1.50	Exp
hsa-miR-3611	Improver	up	up	11	1.59E-01	1.41	Exp
hsa-miR-3611	Improver	up	down	10	2.52E-02	2.05	Exp
hsa-miR-4279	Improver	up	down	54	1.36E-01	1.16	2
hsa-miR-4290	Improver	up	up	7	6.65E-02	1.96	3
hsa-miR-4299	Improver	up	down	25	1.98E-01	1.20	2
hsa-miR-4419b	Improver	up	down	59	5.77E-02	1.23	2
hsa-miR-4421	Improver	up	down	3	9.23E-02	2.79	Exp

hsa-miR-4473	Improver	up	up	12	2.53E-02	1.90	Exp
hsa-miR-4478	Improver	up	down	58	1.02E-01	1.18	2
hsa-miR-4530	Improver	up	down	54	1.48E-01	1.16	2
hsa-miR-4536-3p	Improver	down	down	8	4.00E-02	2.08	2
hsa-miR-4667-5p	Improver	up	down	11	2.43E-02	1.98	3
hsa-miR-4682	Improver	up	down	13	2.20E-02	1.89	3
hsa-miR-4698	Improver	up	down	131	8.64E-05	1.37	2
hsa-miR-4698	Improver	up	down	46	2.14E-03	1.56	3
hsa-miR-4698	Improver	up	up	7	1.06E-01	1.75	Exp
hsa-miR-4701-5p	Improver	down	down	52	6.01E-02	1.25	2
hsa-miR-4701-5p	Improver	down	down	6	1.58E-01	1.65	3
hsa-miR-4709-3p	Improver	up	down	68	1.10E-02	1.32	2
hsa-miR-4712-3p	Improver	up	down	36	6.60E-02	1.30	2
hsa-miR-4732-3p	Improver	up	up	42	1.40E-01	1.19	2
hsa-miR-4732-3p	Improver	up	down	28	1.19E-01	1.27	2
hsa-miR-4732-3p	Improver	up	up	8	4.72E-02	2.00	3
hsa-miR-4739	Improver	up	down	13	1.91E-01	1.32	3
hsa-miR-4747-5p	Improver	up	down	63	5.29E-02	1.23	2
hsa-miR-4747-5p	Improver	up	down	16	4.38E-02	1.61	3
hsa-miR-4762-5p	Improver	up	up	62	1.60E-01	1.14	2
hsa-miR-4762-5p	Improver	up	down	44	5.07E-02	1.29	2
hsa-miR-4762-5p	Improver	up	up	24	2.86E-02	1.52	3
hsa-miR-4800-3p	Improver	up	down	3	1.64E-01	2.14	2
hsa-miR-483-3p	Improver	up	down	9	5.53E-02	1.86	2
hsa-miR-485-3p	Improver	up	down	37	1.14E-02	1.48	2
hsa-miR-485-3p	Improver	up	up	11	1.35E-01	1.46	Exp
hsa-miR-485-3p	Improver	up	down	7	1.94E-01	1.49	Exp
hsa-miR-490-3p	Improver	up	down	32	2.15E-02	1.46	2
hsa-miR-490-3p	Improver	up	down	10	1.91E-02	2.15	3
hsa-miR-490-3p	Improver	up	up	4	7.89E-03	4.89	4
hsa-miR-490-3p	Improver	up	down	2	9.16E-02	3.91	4
hsa-miR-490-3p	Improver	up	down	14	4.82E-03	2.21	Exp
hsa-miR-516b-5p	Improver	up	up	66	1.41E-01	1.14	2
hsa-miR-516b-5p	Improver	up	down	46	5.48E-02	1.28	2
hsa-miR-516b-5p	Improver	up	down	12	1.32E-01	1.44	3
hsa-miR-516b-5p	Improver	up	down	4	5.11E-02	2.86	4
hsa-miR-5187-3p	Improver	up	down	47	1.32E-02	1.40	2
hsa-miR-589-5p	Improver	down	down	8	1.39E-01	1.57	3
hsa-miR-589-5p	Improver	down	down	3	2.88E-02	4.46	4
hsa-miR-597	Improver	down	down	8	1.60E-01	1.52	2
hsa-miR-597	Improver	down	down	4	1.55E-02	4.13	3
hsa-miR-642b-5p	Improver	up	down	21	3.89E-02	1.52	2
hsa-miR-642b-5p	Improver	up	down	6	8.50E-02	1.97	3
hsa-miR-660-3p	Improver	up	down	44	1.06E-01	1.21	2
hsa-miR-660-3p	Improver	up	down	19	5.10E-02	1.51	Exp
hsa-miR-665	Improver	up	down	55	1.90E-01	1.13	2
hsa-miR-744-5p	Improver	up	down	20	1.80E-01	1.25	Exp