

Ind vs NInd			
miRNA	<i>p</i> -value	Fold change	Regulation
rno-miR-770-3p	0.0495	-5.3917	down
rno-miR-346	0.0463	-5.0284	down
rno-miR-201-5p	0.0495	5	up
rno-miR-598-5p	0.0495	-4.7671	down
rno-miR-375-3p	0.0495	4.5716	up
rno-miR-377-5p	0.0495	-3.1195	down
rno-miR-3558-5p	0.0495	3.0575	up
rno-miR-412-5p	0.0495	-3.053	down
rno-miR-376a-3p	0.0495	-2.934	down
rno-miR-147	0.0495	2.8676	up

**Table S1.** miRNAs with the largest fold change in expression in Ind compared with NInd at day 4 as determined by a Mann-Whitney U test. All data analysis carried out on three independent replicates. Fold change cut-off >1.5,  $p \leq 0.05$ .

Ind+S vs NInd			
miRNA	<i>q</i> -value	Fold change	Regulation
rno-miR-3553	0.0466	8.481	up
rno-miR-410-5p	0.0467	8	up
rno-miR-182	0.0466	3.6954	up
rno-miR-377-3p	0.0466	3.3264	up
rno-miR-1247-3p	0.0466	-3.2453	down
rno-miR-708-3p	0.0454	-3.093	down
rno-miR-758-3p	0.0496	3.0928	up
rno-miR-10a-5p	0.0466	3.011	up
rno-miR-543-3p	0.0466	2.932	up
rno-miR-540-3p	0.0466	2.7322	up

**Table S2.** miRNAs with the largest fold change in expression in Ind+S compared with NInd at day 4 as determined by a moderated t-test in combination with Storey's bootstrapping method. All data analysis carried out on three independent replicates. Fold change cut-off >1.5,  $q \leq 0.05$ .

Ind+A vs NInd			
miRNA	q-value	Fold change	Regulation
rno-miR-881-3p	5.56E-04	603.906	up
rno-miR-741-3p	2.53E-04	249.7982	up
rno-miR-871-3p	2.53E-04	213.5208	up
rno-miR-871-5p	0.001	199.2512	up
rno-miR-743b-3p	0.001	194.4895	up
rno-miR-743a-3p	2.53E-04	178.295	up
rno-miR-463-5p	0.001	161.3718	up
rno-miR-743b-5p	4.06E-04	98.8655	up
rno-miR-3580-3p	0.002	51.3771	up
rno-miR-471-5p	2.53E-04	36.765	up

**Table S3.** miRNAs with the largest fold change in expression in Ind+A compared with NInd at day 4 as determined by moderated t-test in combination with Storey's bootstrapping. All data analysis carried out on three independent replicates. Fold change cut-off >1.5,  $q \leq 0.05$ .

Ind+S vs Ind			
miRNA	q-value	Fold change	Regulation
rno-miR-346	0.0144	9.0318	up
rno-miR-3553	0.0231	7.1433	up
rno-miR-412-5p	0.0231	7.0871	up
rno-miR-410-5p	0.0329	6.8276	up
rno-miR-377-5p	0.0326	6.2164	up
rno-miR-183-5p	0.0311	5.6106	up
rno-miR-770-3p	0.0276	5.4077	up
rno-miR-377-3p	0.0156	4.9179	up
rno-miR-6331	0.0184	4.6497	up
rno-miR-667-5p	0.0215	4.5881	up

**Table S4.** miRNAs with the largest fold change in expression in Ind+S compared with Ind at day 4 as determined by moderated t-test in combination with Storey's bootstrapping. All data analysis carried out on three independent replicates. Fold change cut-off >1.5,  $q \leq 0.05$ .

Ind+A vs Ind			
miRNA	<i>q</i> -value	Fold change	Regulation
rno-miR-881-3p	0.0066	273.9668	up
rno-miR-743b-3p	0.002	240.7617	up
rno-miR-871-3p	0.003	214.3537	up
rno-miR-743a-3p	1.94E-04	191.8932	up
rno-miR-463-5p	0.0015	175.1376	up
rno-miR-741-3p	0.0015	172.5662	up
rno-miR-871-5p	0.003	153.8468	up
rno-miR-743b-5p	0.001	86.0507	up
rno-miR-3580-3p	0.0023	51.3771	up
rno-miR-471-5p	1.94E-04	36.765	up

**Table S5.** miRNAs with the largest fold change in expression in Ind+A compared with Ind at day 4 as determined by moderated t-test in combination with Storey's bootstrapping. All data analysis carried out on three independent replicates. Fold change cut-off >1.5,  $p \leq 0.05$ .

miRNA	Fold change				Notes/reason for selection	Reference	% Sequence similarity with human ortholog
	Ind+S vs NInd	Ind+A vs NInd	Ind+S vs Ind	Ind+A vs Ind			
<b>rno-miR-200b-3p</b>	-	2.598	-	1.559	Differentially regulated in Ind+A compared with NInd and Ind  Controlled by DNMT3A	Zhao et al., 2018	95.70
<b>rno-miR-205</b>	-2.06	3.11	-	3.98	Inhibition of miR-205 enhances osteogenic abilities by upregulating <i>Bsp</i> and <i>Opn</i>  Is one of many <i>Runx2</i> -targeting miRNAs suggested to be involved in osteogenesis and chondrogenesis	Hu et al., 2015  Zhang, et al., 2011	95.6%
<b>rno-miR-221-5p*</b>	1.732	1.667	-	-	Differentially regulated in two of three groups  Inhibition of microRNA-221-5p induces osteogenic differentiation of BMMSCs via upregulation of <i>SMAD3</i>	Fan et al., 2019	95.70

miRNA	Fold change				Notes/reason for selection	Reference	% Sequence similarity with human ortholog
	Ind+S vs NInd	Ind+A vs NInd	Ind+S vs Ind	Ind+A vs Ind			
<b>rno-miR-182</b>	3.695	2.056	2.907	-	Downregulated miR-182-5p promotes the proliferation and differentiation of osteoblasts in osteoporotic rats through Rap1-MAPK signalling	Pan et al., 2018	92
<b>rno-miR-346</b>	-	-	9.032	-	Highest differentially regulated in Ind+S vs Ind		87
<b>rno-miR-881-3p</b>	-	603.91	-	273.97	Highest differentially regulated in Ind+A vs Ind		N/A

**Table S6.** Six miRNAs chosen for validation using qRT-PCR. The fold change of each miRNA in each of the 5 experimental pairings as determined by A moderated t-test combined with Storey's bootstrapping method is shown, as well as the percentage sequence identity each miRNA shares with its human ortholog. rno-miR-881-3p does not have a known human ortholog. miR-221-5p was not found to be differentially regulated in any experimental group when using the moderated t-test, however the less stringent Mann-Whitney U test determined it to be differentially expression in Ind+S and Ind+A compared with Ind.