

## **MiR-218 targets MeCP2 and inhibits heroin seeking behavior**

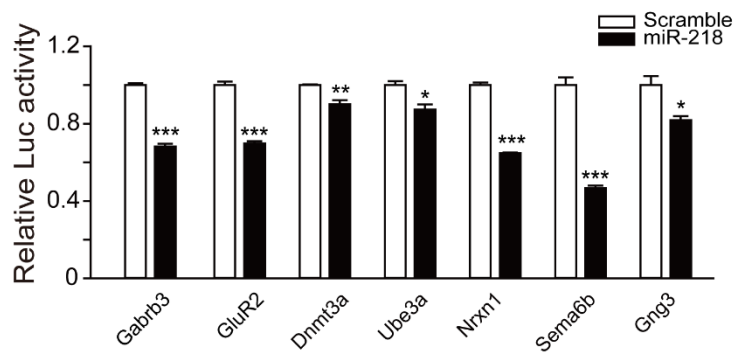
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**Fig. S1**



**Supplementary Figure 1:** Luciferase validation of potential miR-218 targets in addiction-related pathway. Relative luciferase activity with the Gabrb3, GluR2, Dnmt3a, Ube3a, Nrxn1, Sema6b, Gng3 3' UTR in 293T cells co-transfected with scramble or miR-218 mimic synthetic RNA (n = 3 for each group, \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001 vs scramble).

**Supplementary Table 1.** Putative addiction-related miRNA families identified by NP method.

<b>Symbol</b>	<b>Z score</b>	<b>Targets</b>	<b>maxNPES</b>	<b>Leading edge targets</b>
<b>miR-128-3p</b>	1.5027	764	0.312	<i>Mapk1, Stat1, E2F3, Grm5, Gria1, Gabbr2, Sp1, Cacna1A, Cnr1, Gad1, Creb1, Fosb, Pparg, Ppp1Cc, Slc6A1, Grin2D, E2F6, Nfat5, Lrrfip1, Nptx1, Kcna1, Syt1, Ncam1, Nova1, Rap1B, Gabrb1, Rps6Ka5, Grb2, Nf1, Mapk14, Atp2B1, Thrb</i>
<b>miR-181-5p</b>	0.0993	758	0.3046	<i>Mapk1, Fos, Gria2, Yy1, Grm5, Sp1, Drd1, Gnaq, Cnr1, Creb1, Map2K1, Bcl2, Homer1, Nfat5, Lrrfip1, Tnf, Ppp1Cb, Nr3C1, Mef2A, Ywhag, Hspa5, Atxn3, Cntn4, Nova1, Rap1B, Gabrb1, Mapt, Gnao1, Grid1, Atp2B1, Gabra1, Gabra4, Dusp6, Thrb, Dusp5, Zeb1</i>
<b>miR-9-5p</b>	0.2388	959	0.2716	<i>Drd2, Irf1, Abat, Srf, Gabbr2, Gabrb2, Gad1, Prkca, Cnp, Nptx1, Scn2B, Kcna1, Gchl, Atxn3, Syt1, Cntn4, Rap1B, Nfkb1, Atf1</i>
<b>miR-27-3p</b>	0.4497	860	0.2603	<i>Stat1, Grm5, Camk2A, Slc1A2, Sp1, Cacna1A, Creb1, Fosb, Pparg, Ppp1Cc, Slc6A1, Grin2D, Camk4, E2F6, Nfat5, Syt1, Ncam1, Nova1, Gabrb1, Rps6Ka5, Mapt, Grb2, Nf1, Mapk14, Atp2B1, Thrb, Dusp5, Tbp</i>
<b>miR-129-5p</b>	0.6052	326	0.2459	<i>Mapk1, Stat1, Grm5, Gabbr2, Cacna1A, Gnaq, Glul, Kdm2B, Camk4, Mef2A, Nptx1, Syt1, Rps6Ka5, Ybx1, Sp3</i>
<b>miR-218-5p</b>	0.7449	677	0.2393	<i>Gria2, Yy1, Tac1, Sp1, Gabrb2, Creb1, Ppp1Cc, Slc6A1, Lrrfip1, Ppp1Cb, Kcnd2, Scn2B, Kcna1, Syt1, Gnai2, Plcg1, Gnao1, Thrb, Dusp5</i>
<b>miR-135-5p</b>	0.0898	528	0.2281	<i>Sp1, Gabrb2, Slc6A4, Plcb1, Ppp1Cc, Nfat5, Lrrfip1, Elk3, Adcyap1, Mef2A, Nptx1, Ywhag, Scn2B, Syt1, Gabrb1, Plcg1, Rps6Ka5, Mapk10, Sp3, Nefm, Cacna1D, Thrb, Dusp5, Dusp8, Mef2C, Tfap2A</i>
<b>miR-148-3p/152-3p</b>	0.8809	450	0.2244	<i>E2F3, Grin2A, Camk2A, Cnr1, Fosb, Kdm2B, Homer1, Nfat5, Ppp1Cb, Nptx1, Atxn3, Syt1, Ncam1, Cntn4, Nova1, Rps6Ka5, Gadd45A, Erbb3, Dusp8</i>
<b>miR-34-5p/449-5p</b>	0.7546	425	0.217	<i>Mycn, E2F3, Yy1, Htr2C, Gnaq, Map2K1, Bcl2, Crhr1, Slc6A1, Prkacb, Camk4, Scn2B, Syt1, Gnai2, Casp2, Gabrb1, Plcg1, Mapt, Gnao1, Grid1</i>

<b>miR-144-3p</b>	0.5218	588	0.2166	<i>Mycn, Fos, Grm5, Gabrb2, Creb1, Fosb, Tall, Egfr, Nr3C1, Mef2A, Nptx1, Adrb1, Kcna1, Noval, Rap1B</i>
<b>miR-23-3p</b>	0.0427	702	0.2117	<i>Irf1, Stat1, Grm5, Htr2A, Htr2C, Fosb, Crebbp, Pgr, Ppp3Ca, Lpar1, Ppp1Cb, Adcyap1, Mef2A, Ywhag, Atxn3, Rap1B, Ptk2B, Dusp5, Zeb1, Pten, Mef2C, Stat5B</i>
<b>miR-153-3p</b>	2.0622	563	0.2115	<i>E2F3, Htr1F, Plcb1, Bcl2, Crebbp, Kdm2B, Syn1, Ppp3Ca, Mef2A, Kcna1, Syt1, Noval, Igf1R, Rps6Ka5, Ryr3, Sp3, Grb2, Nf1, Snca, Pten, Mef2C, Fyn, Myb</i>
<b>miR-204-5p/211-5p</b>	1.1274	338	0.2052	<i>Mapk1, Gabbr2, Gnaq, Creb1, Bcl2, Nfat5, Nr3C1</i>
<b>miR-145-5p</b>	0.1917	472	0.1894	<i>Mycn, E2F3, Slc1A2, Htr2A, Sp1, Dlg4, Pmp22, Ppp3Ca, Adcyap1, Plce1, Ywhag, Cntn4, Igf1R, Sp3, Cacna1D, Dusp6, Gdnf</i>
<b>miR-139-5p</b>	0.2443	244	0.1872	<i>Fos, Grin2A, Gabbr2, Jun, Homer1, Pmp22, Nfat5, Nptx1, Ywhag, Ppp2Ca, Rap1B, Igf1R,</i>
<b>miR-142-5p</b>	0.1518	539	0.1821	<i>Mycn, Fos, Yy1, Srf, Camk2A, Htr2A, Drd1, Nfat5, Ppp3Ca, Arhgap35</i>
<b>miR-22-3p</b>	0.7664	319	0.1813	<i>Grm5, Gabbr2, Sp1, Creb1, Slc6A1, Homer1, Nr3C1, Faslg, Mapk14, Erbb3</i>
<b>miR-24-3p</b>	0.6480	345	0.1807	<i>Gabbr2, Sp1, Gad1, Hap1, Prkca, Nfat5, Nptx1, Rap1B, Nefm, Mapk14, Erbb3, IL1R1, Dusp8, Per1</i>
<b>miR-143-3p</b>	2.0258	225	0.1707	<i>Htr2A, Htr2C, Cacna1A, Bcl2, Noval, Igf1R, Erbb3</i>
<b>miR-7-5p</b>	0.8035	308	0.1673	<i>Grin2A, Sp1, Plcb1, Raf1, Gabbr1, Scn2B, Vdac1, Snca, Gabra1, Vdac3</i>
<b>miR-132-3p/212-3p</b>	0.7259	255	0.1631	<i>Mapk1, Slc6A1, Nfat5, Adcyap1, Mef2A, Ywhag, Noval, Mapt, Wt1</i>
<b>miR-138-5p</b>	0.1298	393	0.1604	<i>Creb1, Rela, Casp3, Ywhah, Arhgap35, Nptx1, Per2, Scn1B, Gnai2, Noval, Gabrb1, Grid1, Thrb, Mapk6</i>
<b>miR-10-5p</b>	0.5119	203	0.1486	<i>E2f3, Bdnf, Gabrb2, Creb1, Nfat5</i>
<b>miR-338-3p</b>	0.8484	221	0.1452	<i>Stat1, Camk2A, Gnaq, Kcnd2, Noval, Mapt, Ppm1B</i>
<b>miR-193-3p</b>	9.1819	133	0.1442	<i>Mycn</i>
<b>miR-155-5p</b>	0.9142	252	0.1442	<i>Fos, Bdnf, Rela, Nfat5, Mef2A</i>
<b>miR-221-3p/222-3p</b>	0.9929	260	0.1396	<i>Fos, Nfat5</i>
<b>miR-194-5p</b>	0.4426	244	0.1363	<i>Stat1, E2F3</i>
<b>miR-365-3p</b>	1.3728	178	0.1245	<i>Bdnf, Ywhah, Nr3C1, Cntn4</i>
<b>miR-140-5p</b>	0.0067	212	0.1228	<i>Bcl2L1, Ppp1Cc, Nfat5, Ywhag, Rap1B, Igf1R</i>

<b>miR-31-5p</b>	0.6497	210	0.1144	<i>Slc1A2, Homer1, Ppp3Ca</i>
<b>miR-210-3p</b>	0.8070	19	0.1047	<i>Bdnf, Mef2A</i>
<b>miR-150-5p</b>	0.0408	142	0.1003	<i>Sp1, Prkca, Ppp2Cb, Nefm, Gabrg2, Zeb1, Myb</i>
<b>miR-146-5p</b>	0.5895	120	0.0984	<i>Kdm2B, Syt1, Noval, Grid1, Gdnf, Per1, Rel</i>
<b>miR-208-3p</b>	0.6935	133	0.0942	<i>Ppp3Cb, Scn2B, Noval, Ybx1, Sp3, Gabral, Mapk6</i>
<b>miR-18-5p</b>	0.0425	166	0.0941	<i>Prkacb, Nfat5, Nr3C1, Kcna1, Igf1, Rasa2,</i>
<b>miR-223-3p</b>	0.9148	178	0.0918	<i>Mpz, E2F1, Rbpj, Igf1R, Sp3, Atp2B1, Zeb1, Mef2C</i>
<b>miR-490-3p</b>	0.4216	96	0.0509	<i>Slc1A3</i>
<b>miR-99-5p/100-5p</b>	-3.8616	38	0.048	<i>Ppp1Cb, Igf1R</i>