ABSTRACT

In obesity and type 2 diabetes, numerous genes are differentially expressed, and microRNAs are involved in transcriptional regulation of target mRNAs, but miRNAs critically involved in the appetite control are not known. Here, we identified upregulation of miR-342-3p and its host gene *Evl* in brain and adipose tissues in C57BL/6 mice fed with high fat-high sucrose (HFHS) chow by RNA sequencing. *Mir342* (-/-) mice fed with HFHS chow were protected from obesity and diabetes. The hypothalamic arcuate nucleus neurons co-express *Mir342* and EVL. The percentage of activated $NPY^{+}pSTAT3^{+}$ neurons were reduced, while $POMC^{+}pSTAT3^{+}$ neurons increased in *Mir342* (-/-) mice and they demonstrated the reduction of food intake and amelioration of metabolic phenotypes. *Snap25* was identified as a major target gene of miR-342-3p and the reduced expression of *Snap25* may link to functional impairment hypothalamic neurons and excess of food intake. The inhibition of miR-342-3p may be a potential candidate for miRNA-based therapy.