

SUPPLEMENTARY MATERIAL

Table S1. Definition and example of high_confidence and low_confidence level record

Category		Definition	Example
miR2Epi	High_confidence level record	Records ought to clearly elucidate that miRNA could affect epigenetic states through targeting some known epigenetics-associated enzymes or proteins.	Nguyen <i>et al.</i> showed that DNMT-3a and DNMT-3b are directly targeted by miR-29b with luciferase reporter assay and their expression is repressed by miR-29b. Additionally, the downregulation of DNMT-3a and DNMT-3b caused by miR-29b could lead to loss of promoter methylation of E-cadherin and Cdh2 and activation of them. [PubMed ID: 23266889]
	Low_confidence level record	Records only demonstrate that miRNA can target epigenetics-associated enzymes or proteins (indicating that the miRNA has regulatory potential), but did not offer definite and enough evidences to exhibit the regulating process that miRNA can control states of epigenetics. In addition, the records that discovering the regulatory relationship between epigenetics and miRNA merely based on high-throughput technology are also categorized as the low_confidence level.	Noonan <i>et al.</i> only discovered that miR-449a can directly target histone deacetylase-1 and consequently regulate their expression. Even through miR-449a owns potential to affect the histone modification, the author did not provide enough evidence to prove that the miR-449a actually lead to the change of epigenetic state. [PubMed ID: 19252524]
Epi2miR	High_confidence level record	Records not only certified the existence of epigenetics on the miRNA gene, but also discovered that the	Brueckner <i>et al.</i> found that the upstream CpG island of let-7a-3 was hypermethylated

		<p>epigenetic modification of miRNA is associated with the expression of the corresponding miRNA.</p>	<p>in HCT116 cells and lung tissue samples. They also demonstrated that let-7a-3 was up-regulated in cells that had been treated with the DNA methyltransferases inhibitor. Finally, the analysis of genomic DNA from DNA methyltransferase knockout cell lines showed that let-7a-3 methylation is cooperatively maintained by the DNA methyltransferases DNMT-1 and DNMT-3b. [PubMed ID: 17308078]</p>
	Low_confidence level record	<p>Records only presented the occupancy of epigenetic modification on the miRNA or epigenetics drug can affect expression of the miRNA, but did not completely certify that the epigenetic modification of miRNA can regulate the corresponding miRNA's expression. In addition, the records that discovering the regulatory relationship between epigenetics and miRNA merely based on high-throughput technology are also categorized as the low_confidence level.</p>	<p>Pallasch <i>et al.</i> merely presented that promoter of miR-139 show significant gain of methylation in chronic lymphocytic leukemia. However, they did not completely demonstrate that the low expression of miR-139 is actually in the control of its promoter methylation. [PubMed ID: 19692702]</p>