RVG-exosome delivered MOR-RNAi rescues drug addiction

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MiRNAs are a class of naturally occurring small non-coding RNAs that have been linked to biological possesses and diseases development. In the previous study, Chen-Yu Zhang and colleagues have reported that expression profile of circulating miRNAs in human and other animals are the novel class of biomarkers for diagnosis of cancer and other diseases. Furthermore, the same group has shown that cell selectively packages miRNA into exosomes and secreted miRNAs in exosomes were able to be delivered into target cells and modulated the biological functions of these cells via repression of miRNA target gene.

In the present study, in order to deliver siRNA passing through blood-brain barrier (BBB) and then sufficiently getting into brain, they express signal domain of rabies viral glycoprotein (RVG) in exosome membrane. The RVG-exosome-delivered RNAi against opioid receptor mu (MOR) sufficiently down-regulates MOR in mouse brain, and recuses opioid relapse.

This work is important for the following reasons:

1) This is the first time to demonstrate that MOR is down-regulated by IV injection of MV-RNAi in vivo. The down-regulation of MOR significantly abolishes morphine relapse. Since MOR-RNAi may serve as a more effective treatment for drug addiction compared with other options such as naltrexone and methadone, it provides a new strategy to control drug addiction, 2) RVG-exosome-delivered RNAi also shows the potential to deliver other small RNA (microRNA/RNAi) to across the

blood brain barrier for treatment of more CNS diseases.

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