VIROLOGY

Qian, X., et al. (2016). "Exosomal MicroRNAs Derived From Umbilical Mesenchymal Stem Cells Inhibit Hepatitis C Virus Infection." Stem Cells Transl Med 5(9): 1190-1203.

UNLABELLED: : Hepatitis C virus (HCV) is a significant global public health problem, causing more than 350,000 deaths every year. Although the development of direct-acting antivirals has improved the sustained virological response rate in HCV patients, novel anti-HCV agents with higher efficacy as well as better tolerance and cheaper production costs are still urgently needed. Cell-based therapy, especially its unique and strong paracrine ability to transfer information to other cells via extracellular vesicles such as exosomes, has become one of the most popular therapeutic methods in recent years. In our study, exosomes secreted from umbilical mesenchymal stem cells (uMSCs), which are widely used in regenerative medicine, inhibited HCV infection in vitro, especially viral replication, with low cell toxicity. Our analysis revealed that microRNAs (miRNAs) from uMSC-derived exosomes (uMSC-Exo) had their unique expression profiles, and these functional miRNAs, mainly represented by let-7f, miR-145, miR-199a, and miR-221 released from uMSC-Exo, largely contributed to the suppression of HCV RNA replication. These four miRNAs possessed binding sites in HCV RNA as demonstrated by the target prediction algorithm. In addition, uMSC-Exo therapy showed synergistic effect when combined with U.S. Food and Drug Administration-approved interferon-alpha or telaprevir, enhancing their anti-HCV ability and thus improving the clinical significance of these regenerative substances for future application as optimal adjuvants of anti-HCV therapy. SIGNIFICANCE: This work reported, for the first time, the identification of stem cell-derived exosomes of antiviral activity. Umbilical mesenchymal stem cell-secreted exosomes inhibited hepatitis C virus infection through transporting a mixture of microRNAs complementing the viral genomes to the host cells. This finding provides insights and prospects for physiologically secreted substances for antiviral therapy.