

## Shennao fuyuan decoction and hUCMSC-exo combination therapy promotes lipid and atherosclerosis pathway activation and improves brain injury in middle cerebral artery occlusion rats

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Human umbilical cord mesenchymal stem cell-derived exosomes (hUCMSC-exo) decrease the mortality rates associated with brain injuries. Its combination with Shennao fuyuan decoction (SFD), a traditional Chinese medicine formulation for ischemic stroke treatment, additionally augments neural deficit repair in rats post-cerebral ischemia. Nonetheless, there is a notable need for more comprehensive research into the exact mechanisms by which this combined treatment ameliorates brain injuries. Consequently, we conducted thorough research on the mechanisms of action of these entities, utilizing network pharmacology approaches and a rat model of middle cerebral artery occlusion (MCAO). Our findings identified the hsa05417: Lipid and atherosclerosis pathway as the primary channel through which SFD impacts the cardiovascular system. The integrated treatment of SFD and hUCMSC-exo attenuated TNF and HSP90AA1 expression and elevated IL6 and GSK3B levels in the brains of rats subjected to MCAO. Moreover, the discrete utilization of hUCMSC-exo in conjunction with SFD reduced cerebral infarction and diminished tissue damage in rats with MCAO. Our investigation has revealed that the coordinated use of hUCMSC-exo and SFD may influence the TNF, HSP90AA1, IL6 and GSK3B targets, thereby managing the lipid and atherosclerosis pathway and lessening cerebral harm in rats afflicted by MCAO.

**Keywords:** Atherosclerosis, Cerebral infarction, Exosomes, Traditional Chinese medicine