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## **Alternative, Complementary & Integrative Medicine**

### **Opinion**

# A Famous Chinese Prescription That Promotes Hcn4 Activity in Bone Marrow Mesenchymal Stem Cells is Shenfu Injection: Opinion

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Sick Sinus Syndrome (SSS) refers to a group of heart rhythm disorders caused by problems relating to the sinus node. Currently, there is no effective treatment for SSS, and an electronic pacemaker is required to support heart function in SSS patients. However, electronic pacemakers are associated with several defects. For example, external magnetic noise commonly interferes, leading to complications. In addition, some patients, especially children with congenitals inoatrial node dysfunction, are not suitable subjects for pacemaker insertion. Therefore, the search for new therapeutic strategies for treating cardiovascular diseases has become imperative. Shenfu injection (SFI), a Chinese herbal medicine, is effective in improving bradyarrhythmia. However, the underlying mechanism of SFI's therapeutic effect remains elusive.

In this study, We investigated the effects of Shenfu Injection (SFI) on HCN4 activity in Bone Marrow Mesenchymal Stem Cells (BMSCs). The sample of BMSCs was divided into six groups: a control group, a high-dose SFI group (0.25ml/ml), a middle-dose SFI group(0.1ml/ml), a low-dose SFI group (0.05ml/ml), an adenovirus-encoded control vector group, andanadeno virus-encoded HCN4 group. Cell ultra structure was observed using a transmission electron microscope. Quantitative Reverse Transcription PCR (RTqPCR) was performed to detect HCN4 expression, and HCN4 activity was detected using the whole-cell patch clamp technique. An enzyme-linked immunosorbent assay was performed to detect cAMP content. Application of flow cytometry confirmed that the isolated cells showed BMSC-like phenotypes. Differentiation of BMSCs in both the SFI and the adenovirus-encoding HCN4 groups occurred according to the cellular ultra structure. Application of the whole-cell patch clamp technique revealed that SFI could activate the inward pacing current of BMSCs in a concentration-dependent manner. The RT-qPCR results showed that HCN4 expression was significantly higher in the high-dose SFI group than in the medium and low-dose groups, whereas the cAMP content in the over expressed HCN4 group decreased significantly; this content in the high-dose SFI group increased significantly. In conclusion, SFI promotes HCN4 activity in BMSCs, which could explain its treatment effect when administered to patients with cardio vascular diseases. At present, the research group is conducting an in-depth study on the SFI for sinus node syndrome.

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