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MicroRNA-23a Participates in Estrogen Deficiency Induced Gap Junction Remodeling of Rats by Targeting GJA1

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Abstarc :

Increased incidence of arrhythmias in women after menopause has been widely documented, which is considered to be related to estrogen (E2) deficiency induced cardiac electrophysiological abnormalities. However, its molecular mechanism remains incompletely clear. In the present study, we found cardiac conduction blockage in post-menopausal rats. Thereafter, the results showed that cardiac gap junctions were impaired and Connexin43 (Cx43) expression was reduced in the myocardium of post-menopausal rats. The phenomenon was also observed in ovariectomized (OVX) rats, which was attenuated by E2 supplement. Further study displayed that microRNA-23a (miR-23a) level was significantly increased in both post-menopausal and OVX rats, which was reversed by daily E2 treatment after OVX. Importantly, forced overexpression of miR-23a led to gap junction impairment and Cx43 downregulation in cultured cardiomyocytes, which was rescued by suppressing miR-23a by transfection of miR-23a specific inhibitory oligonucleotide (AMO-23a). GJA1 was identified as the target gene of miR-23a by luciferase assay and miRNA-masking antisense ODN (miR-Mask) assay. We also found that E2 supplement could reverse cardiac conduction blockage, Cx43 downregulation, gap junction remodeling and miR-23a upregulation in post-menopausal rats. These findings provide the evidence that miR-23a mediated repression of Cx43 participates in estrogen deficiency induced damages of cardiac gap junction, and highlights a new insight into molecular mechanism of post-menopause related arrhythmia at the microRNA level.

Key Word :
Connexin43, Post-menopause, Estrogen, MicroRNA-23a, Arrhythmia

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