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The G protein-coupled receptor 30 (GPR30): A novel candidate for Diabetic cardiomyopathy in postmenopausal women

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Diabetic Cardiomyopathy is characterized by significant changes in cardiac metabolism and are increased in postmenopausal women, which emphasize the role of 17β-Estradiol (E2). Despite this, there are few safe pharmacological treatments for these disorders. The G Protein-coupled Receptor 30 (GPR30), which mediates the non-genomic effects of E2, has beneficial cardiac effects in both Type 2 Diabetes (T2D) and menopause. Based on pharmacological approaches, a growing body of experimental evidence highlights the role of GPR30, in particular, the adjustment of cardiometabolic function, but its exact mechanism is not fully understood. Generally, our results showed that T2D leads to cardiovascular dysfunction, possibly due to a change in the cardiac CD36, Peroxisome Proliferator-Activated Receptor α (PPARα), Hexokinase 2 enzyme (HK2), Glucose Transport 4 (GLUT4) and inflammatory and anti-inflammatory cytokines. Furthermore, induction of the menopausal model can worsen the effects of diabetes. However, our results showed that the cardiovascular protective mechanism of the GPR30 in addition to correcting lipid and glycaemic profiles, reducing insulin resistance and increase in GPR30 level protein also reduces inflammatory cytokines and increases anti-inflammatory cytokines. Although all inflammatory cytokines are not affected by stimulation or inhibition of GPR30, the ratio of inflammatory to anti-inflammatory cytokines decreases. In relation to changes in cardiac metabolism, our results showed that the stimulation of GPR30 by increasing the expression of PPARα and HK2 leads to a decrease in cardiac content of glycogen, glucose, free fatty acids and lipids. We conclude that G-1 as a GPR30 agonist is a prototype candidate drug for potential translation into clinical applications. It is suggested that in future studies, firstly the role of other estrogen receptors in the cardiovascular protective action of this sex steroid in postmenopausal diabetic animals should be investigated and secondly, the intracellular signalling pathway of the membrane receptor in diabetes should also be investigated.

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