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ESTROGEN RECEPTORS IN CARDIOVASCULAR SYSTEM
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Estrogen (E2) is one of the vital steroid hormone with pleiotropic effects in cardiovascular system (CVS). E2 has been found to exert a variety of beneficial effects on the CVS. Most prominently its important in prevent arterogenesis, thrombosis, cell proliferation, by giving cardio protective effect by inhibit the proliferation of vascular smooth muscle cells (VSMC) and also additionally prevents apoptosis and necrosis of cardiac and endothelial cells, anti-inflammatory agent. In general, by the secretion of this hormone or by hormone replacement therapy, the whole body is in a constant state.

The most significant types of receptors are nuclear receptors (NR) and membrane receptors (MR). ER α and ER β are NR and G-protein coupled ER (GPR30/GPER) is MR. By most researchers, immunoblotting and immunofluorescence with a monoclonal anti E2 receptor antibody shows these ERs are functional in CVS (Richard H. Karas, 1943). 17 β estradiol (E2) is one common form of circulating estrogen (Circ. Res. 2011). One most important process mediated by E2 binding on ERs is nitric oxide (NO) production in endothelial cells, through endothelial cells, through endothelial NO synthase (eNOS), also modulates angiogenesis or vascular permeability via an ER mediated mechanism helps in collagen synthesis, mediate cardiac responses to hypoxia.

ER α , one investigation revealed (Brash L et al, 2018) that E2-ER α binding activated bone morphogenic protein receptor 2 (BMPR2) signaling, which has been identified as a potent effector of cardiac contractile force, by maintaining Right ventricular (RV) function as a cardioprotective effect. And pulmonary artery banding of several rats shows protective effect of E2-ER α against diastolic dysfunction is sex specific. Also it reduces endothelial dysfunction in hypertension, reduces VSMC differentiation and lipid accumulation in atherosclerosis.

ER β , activation of this vital for estrogen-dependent upregulation of both eNOS and inducible NOS (iNOS) in cardiomyocytes, also attenuates cardiac remodeling (Nuedling S et al, 2001). In atherosclerosis, it reduces calcification and VSMC differentiation. In hypertension it reduce vasoconstriction, blood pressure, vascular resistance. In pulmonary hypertension, it controls decrease fibrosis, RV modelling and RV hypertrophy. So far, it is responsible for the anti-hypertrophic, anti-fibrotic and anti-apoptotic activities associated with E2.

G-protein coupled ER (GPR30/GPER), most interestingly, reduces cardiac atrial natriuretic peptide, brain natriuretic peptide and myosin heavy chain levels. And also, mainly, by using agonists G1 (GPR30 agonist), is able to reduce Angiotensin II-induced hypertrophy among neonatal cardiomyocytes, this is how G1 binds to GPER1, a receptor expressed in cardiomyocytes. (Pei H et al, 2019). This activation initiates a cascade of intracellular signalling pathways, and then, after activation, GPER1 stimulated by a specific pathway helps cell growth and survival. G1 enhances the phosphorylation of key proteins like Akt, p70S6K1 and mTOR, which helps counteract the hypertrophic effects of Angiotensin II (Morselli E et al, 2017). G1 reduces the autophagy effect (self-eating) of Angiotensin II.

Overall, ERs regulate the nuclear responses and membrane responses to E2 and change target areas gene expressions, cardioprotective effect, estrogen therapy reduces risk of cardiovascular diseases.