Cardiac β-adrenoceptor subtypes in diabetes: Regulation of cardiac β3-adrenergic receptors

Positive inotropic action of catecholamines is mediated through their interaction with beta-adrenergic receptors (β-ARs), while they can also mediate some deleterious effects, such as cardiac arrhythmias. The β-ARs are members of the G protein-coupled receptors and play important roles in the regulation of heart function. Cellular signaling associated with cardiac β-ARs is composed of coupled mechanism between β1-/β2-AR and Gs proteins with contribution of constitutive β3-AR coupling to Gi proteins. This coupled mechanism further leads to the activation of adenyl cyclase, and thereby increases intracellular cAMP level. However, recent studies have emphasized the contribution of constitutive β1-AR coupling to Gi proteins, thereby initiating additional signal transduction pathways, particularly under physiopathological conditions such as hyperglycemia.

Diabetic cardiomyopathy, as a distinct entity, is recognized due to its diminished responsiveness to β1-AR agonist stimulation in the heart from diabetic rats with no important changes in the responses mediated with β2-AR. Furthermore, an upregulation of β3-AR has been shown in diabetic rat heart with a strong negative inotropic effect on left ventricular function. Experimental data provide evidences that the mechanisms for the negative inotropic effect with β3-AR activation appears to involve activation of a nitric oxide synthase pathway. On the other hand, we have shown that although insulin resistance and cardiomyopathy are developed under high-carbohydrate diet-induced Metabolic Syndrome (MetS), compared to type 1 diabetes, MetS-associated cardiac dysfunction seems not to be associated with any change in β3-AR system, with similar ultrastructural changes into the myocardium.

Biography

Belma Turan has completed her PhD from Ankara University and Post-doctoral studies from INSERM France and University of Ottawa School of Medicine. She is a Professor and the Head of Biophysics department in Ankara University Faculty of Medicine. She has published more than 100 papers in reputed journals and has been serving as an Editorial Board Member of more than 10 international journals. She is also the member of International Academy of Cardiovascular Sciences since 2005. She has supervised over 20 PhD and MSc thesis. Her research interest is focused on cardiac electrophysiology, calcium and zinc ion regulations, oxidant stress, antioxidants and diabetic cardiomyopathy.

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