New Mechanisms of the G Protein-coupled Estrogen Receptor 1 as a Moderator of Cardiovascular Health

Kim Tran

Department of Physiology & Pharmacology, Des Moines University College of Medicine, USA

Plasma estrogen level is closely related to cardiovascular health. Estrogen has complex effects that are both dependent and independent on transcriptional activities and are mediated by at least three estrogen receptors. The novel G protein-coupled estrogen receptor 1 (GPER) regulates many cardiovascular functions such as the control of fat metabolism, insulin resistance and glucose tolerance, and vascular tone and cardiac diastolic functions. However, effects of its activation and mechanisms of action are not well understood. Both Ca2+ entry and Ca2+ efflux are essential in shaping intracellular Ca2+ signals important for cardiovascular functions. Calmodulin, the ubiquitous transducer of Ca2+ signals, is required for the activities of up to 300 intracellular proteins, yet is insufficiently expressed for all its binding sites. This renders an intracellular shortage and dynamic competition for calmodulin across cardiovascular tissues. Factors that control Ca2+ influx, Ca2+ efflux and calmodulin-dependent activities thus plays important roles in the regulation of cardiovascular activities. Key data will be presented on the effects and mechanisms of GPER in the control of Ca2+ entry and efflux, the role of GPER in a feed-forward loop that regulates functional linkage in the network of calmodulin-dependent proteins and its direct involvement in cardiac pressor response. A mechanistic model for the role of GPER as a moderator of cardiovascular functions will be presented. The data and summative model encourage exploitation of GPER activities in the management of cardiovascular morbidity.