

18th Annual Cardiologists Conference

June 19-21, 2017 Paris, France

Endoplasmic reticulum stress, Nrf2 signaling and cardiovascular diseases in a nutshell

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Endoplasmic reticulum (ER) stress is an adaptive mechanism that arises when excessive newly synthesized and/or misfolded polypeptides in the ER lumen exceed its protein folding capacity in response to multiple cellular stress triggers such as oxidative stress, hypoxia and hyperglycemia. The accumulation of unfolded/misfolded proteins activates transcriptional and translational pathways, known as the unfolded protein response (UPR), an adaptive response that helps cell survival by activating a series of intracellular signaling pathways. When the UPR fails to control the level of unfolded/misfolded proteins, ER-initiated apoptotic signaling is induced. Several studies have demonstrated that ER stress occurred in atherosclerotic plaques, particularly in the advanced stages. In addition, ER stress has an important role in cardiac hypertrophy mainly in the transition to heart failure. Interestingly, chronic UPR activation has also been observed in obesity and in diabetes. Oxidative stress that plays a key role in cardiovascular and metabolic disease is counterbalanced by complex antioxidant defense systems regulated by a series of multiple pathways, including the UPR, to ensure that the response to oxidants is adequate. Nuclear factor-E2-related factor (Nrf2) is an emerging regulator of cellular resistance to oxidants; Nrf2 is strictly interrelated with the UPR sensor called pancreatic endoplasmic reticulum kinase. Interventions against ER stress and Nrf2 activators seem to reduce myocardial infarct size and cardiac hypertrophy in animals and to protect against obesity and insulin resistance. These evidences may open new promising therapeutic approaches in chronic cardiovascular and metabolic diseases.

Biography

Anna Fratta Pasini is the Assistant Professor of Internal Medicine at University of Verona Medical School, Verona, Italy. She completed her MD degree at University of Verona. She is Board Certified Specialist in Gastroenterology at University of Verona and Board Certified Specialist in Endocrine Diseases at University of Verona. She is currently a board member of Verona University. She is the Editorial Board Member of *Journal of Cardiology and Therapeutics* and *Journal of Geriatric Cardiology*.

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