A PROTEOMIC APPROACH TO THE MYOCARDIUM OF HYPERTENSIVE-DIABETIC RATS

Lorenzo O.1, Zubiri I.1, Ares-Carrasco S.1, Camafeita E.2, López JA.2, Egido J.1 and Tuñón J.1

1Vascular Pathology laboratory. Fundación Jiménez Díaz Hospital, Autónoma University, Madrid
2Proteomic Unit, National Centre of Cardiovascular Investigations (CNIC), Madrid

Aim: To study the myocardial protein expression secondary to long-term type I diabetes mellitus (DM1).

Methods: Spontaneously hypertensive (SHR) rats received a single streptozotocin injection to develop type I diabetes (DM1). After 28 weeks, DM1/SHR and control normotensive rats were sacrificed and the left ventricles studied by 2DE-DIGE proteomic studied by 2DE-DIGE, MALDI mass spectrometry and biochemical approaches.

Results: Diabetes affects to the myocardium. Glucose impairment and formation of redox molecules induces myocardial fibrosis and apoptosis in the heart. DM1/SHR rats presented hyperglycemia (400 mg/dl) and hypertension (200 mmHg). Rat myocardium showed interstitial and peri-vascular fibrosis and apoptosis. By 2DE-DIGE proteomic assay we found differentiated protein expression in the DM1/SHR myocardium vs. control. Expression of pro-fibrotic factors, as myoenzyme-2 and pro-apoptotic, as anexin-V and C1-citochrome was altered. Anti-oxidants as catalase were also modified. Moreover, mitochondrial metabolism enzymes (for glucose and fatty acids) were deregulated. By biochemical studies, expression of pro-fibrotic molecules Transforming Growth Factor-β (TGFβ), Connective tissue growth factor (CTGF) was enhanced and the TGFβ3-linked transcription factors (p-Smad3/4 and AP-1) were activated. Pro-apoptotic factors FasL, Fas, Bax and cleaved caspase-3 were also augmented (p<0.05). However, the pro-inflammatory molecules, monocyte chemoattractant protein-1 (MCP-1), interleukin-1 (IL-1), and vascular cell adhesion molecule-1 (VCAM-1) were not elevated.

Conclusions: Fibrosis and apoptosis are long-term features of myocardial damage induced by experimental DM1/SHR. New proteomic-identified factors may play a role in these processes. However, inflammation does not seem to be a key feature. Pharmaceutical strategy targeting these factors may be used in hypertensive-diabetic patients.