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## A PROTEOMIC APPROACH TO THE MYOCARDIUM OF HYPERTENSIVE-DIABETIC RATS

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**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<sub>1</sub>), Connective tissue growth factor (CTGF) was enhanced and the TGFβ<sub>1</sub>-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.