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Different proteomic approaches identifies molecular networks underlying cardiac remodelation in western diet-induced obese rats

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Obesity is a complex disease state that is often associated with pathologic changes in the heart, impairing both diastolic and systolic function. Previous studies has investigated potential contributors to this dysfunction, however, the adverse effects of obesity on cardiac function remain incompletely understood. The aim of this study is to identify the myocardial proteins that are differentially expressed between obese rats with cardiac dysfunction and healthy controls, using two different proteomic approaches. Male Wistar rats were distributed into two groups: control (n=13; standard diet) and obese (n=13; Western diet) fed for 41 weeks. The obesity was determined by adipose index. Cardiac function was evaluated by echocardiogram and isolated papillary muscle analysis. The proteomics was based on two-dimensional gel electrophoresis (2DE) followed by mass spectrometry identification (LC-MS/MS) and nano-liquid chromatography with tandem mass spectrometry (nanoLC-MS/MS) followed by label-free quantification. The differentially expressed proteins were subjected to enrichment analysis using the DAVID bioinformatic tool. Obese rats showed increased adiposity index ($p<0.001$). Echocardiographic assessment revealed decreased ejection fraction ($p=0.029$) in obese group. Papillary muscle evaluation indicated both diastolic and systolic dysfunction in baseline condition and in post-rest potentiation maneuver in obese group. A total of 87 myocardial proteins were identified as differentially expressed between control and obese groups, being 46 up- and 41 down-regulated, respectively, in the obese group. Proteins with increased expression are involved in several important biological processes including mitochondrial and peroxisomal fatty acid beta-oxidation, lipid homeostasis (transport and catabolism), oxidative stress pathways and regulation of cardiac muscle contraction by calcium ion signaling. Proteins associated with the cytoskeleton were also elevated. The proteins of lower expression were predominantly from pathways involved in defense against oxidative stress, as well as in glycolysis and amino acid metabolism, tricarboxylic acid cycle, respiratory electron transport chain, ATP metabolic process and cardiac contraction. In conclusion, these two complementary proteomic approaches revealed several molecular alterations in the myocardium of obese rats, enabling a better understanding of the molecular mechanisms involved in cardiac dysfunction, which may suggest some potential novel therapeutic targets for treatment and/or prevention of heart complications in obesity.

Biography

Danielle F Vileigas obtained her BSc Degree in Nutrition (2010) and MSc Degree in Pathophysiology in Internal Medicine (2015) from the São Paulo State University, Brazil respectively. Currently, she is pursuing her PhD student at the same university and has gained an International Fellowship from São Paulo Research Foundation to pursue a research internship during her PhD for 4 months at the Centre for Proteome Research of the University of Liverpool, UK. Her current research involves proteomic approaches to understanding the molecular mechanisms underlying cardiac dysfunction in obesity. She worked on several projects in obesity and cardiology fields.

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