

Comparative proteomics analysis reveals roles for FADD in the regulation of the energy metabolism and proteolysis pathway in mouse

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FAS-associated death domain (FADD) is the key adaptor protein transmitting apoptotic signals mediated by death receptors. FADD also plays essential roles in proliferation, cell cycle and inflammation. The current study shows FADD is probably associated with energy metabolism and proteolysis. It is previously demonstrated that mice bearing the substitution of serine191 to aspartic acid of FADD (FADD-D) exhibit leaner body size than normal and serine191 to alanine (FADD-A) mice, indicating metabolism disorders. A comprehensive strategy of proteomics identification combined with further validation was utilized to identify differentially expressed proteins in three FADD mutant cell lines (FADD, FADD-A and FADD-D). FADD, FADD-A and FADD-D were thought to represent wild type, unphosphorylated and constitutive phosphorylated FADD respectively. 60 spots were determined to be significantly changing due to FADD phosphorylation. Mass spectrometry analysis identified 47 unique proteins. The majority of dysregulated proteins were associated with the generation of precursor metabolites and energy metabolism in mitochondria. Network analysis suggested induction of transcriptional factors that are too low to be detected by two-dimensional gel and identified an enriched cluster of changed proteins involved in cellular metabolic process, including lipid metabolism, fatty acid metabolism, glycolysis, the tricarboxylic acid cycle, and oxidative phosphorylation. In addition, six proteins related to the ubiquitin-proteasome pathway were also identified upregulated in FADD-D cell line. Our further in vivo studies on FADD-D mice strongly confirmed the proteomic results. Together, these studies show that impaired mitochondrial function and proteolysis may play pivotal roles in the dysfunction associated with FADD phosphorylation-induced disorders.

Biography

Zi-Chun Hua has completed his Ph.D in 1994 from Nanjing University and postdoctoral studies from Wadsworth Research Center of New York State Health Department. He is now the Director of the State Key Laboratory of Pharmaceutical Biotechnology and the Chairman of Biochemistry Department, Nanjing University. He was awarded Outstanding Young Investigator by Chinese Nature Science Foundation and Changjiang Scholar Professorship by Ministry of Education of China. He has published more than 164 papers in reputed journals and serving as editorial board members of 7 scientific journals.

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