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Nutritional Proteomics: Investigating molecular mechanisms underlying the health beneficial effect of functional foods

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ABSTRACT:

Objective: We introduce a new technical and conceptual term "nutritional proteomics" by identifying and quantifying the proteins and their changes in a certain organ or tissue dependent on the food intake by utilizing a mass spectrometry-based proteomics technique.

Purpose: Food intake is essentially important for every life on earth to sustain the physical as well as mental functions. The outcome of food intake will be manifested in the health state and its dysfunction. The molecular information about the protein expression change caused by diets will assist us to understand the significance of functional foods. We wish to develop nutritional proteomics to promote a new area in functional food studies for a better understanding of the role of functional foods in health and disease.

Methods: We chose two classes of food ingredients to show the feasibility of nutritional proteomics, omega-3 polyunsaturated fatty acids and omega-6 polyunsaturated fatty acids both of which are involved in the inflammation/anti-inflammation axis. Each class of the polyunsaturated fatty acids was mixed in mouse chow respectively. The liver tissue of mice fed with omega-3 diet or omega-3 diet was analyzed by the state-of-the-art shotgun proteomics using nano-HPLC-ESI-MS/MS. The data were analyzed by the number of differentially expressed proteins that were guaranteed by 1% false discovery rate for protein identification and by the statistical significance of variance evaluated by p-value in two-tailed distribution analysis better than 0.05 (n=4). The differential pattern of protein expression was characterized with Gene Ontology designation.

Results: The data analysis of the shotgun nutritional proteomics identified 2,810 proteins that are validated with 1% FDR. Among these 2,810 proteins, 125 were characterized with statistical

significance of variance ($p<0.05$; $n=4$) between the omega-3 diet and the omega-6 diet by two-tailed distribution analysis. The results illustrate that the dietary influence of omega-3 and omega-6 on protein expression is eminent with the proteins directly responsible for catalytic activity in the "Molecular Function" category, totaling 192 proteins, of Gene Ontology designation. In a similar analysis with regard to the "Cellular Localization" category, protein expression changed the most in the sub-categories of "Cytoplasm", "Membrane", "Nucleus", and "Mitochondrion", totaling 221 proteins. The same analysis with regard to "Biological Process" considering the top four categories, *i.e.*, "Metabolic process", "Regulation of biological (process)", "Response to stimulus", and "Transport" also indicated significant alteration of 182 proteins. These results illustrate a robust influence of dietary elements, omega-3 or omega-6 polyunsaturated fatty acids, on the protein expression in mouse liver.

Conclusions: Application of nutritional proteomics to the dietary effect of omega-3 polyunsaturated fatty acids compared to that of omega-6 on mouse liver revealed; 1) significant number of proteins are altered between the two diets dependent on the classes of polyunsaturated fatty acids, omega-3 or omega-6, in the diet. The change of protein expression is likely to carry the molecular information that we could possibly decipher, leading to a better understanding of the role of omega-3 polyunsaturated fatty acids in inflammatory/anti-inflammatory process. The results corroborate the concept and utility of nutritional proteomics that should be developed as a part of functional food studies with regard to other dietary types.

Keywords: Nutritional proteomics, functional foods, mass spectrometry, genome database, cellular signaling, omega-3 and omega-6 polyunsaturated fatty acids