

【Grant-in-Aid for Scientific Research(S)】
Biological Sciences (Agricultural sciences)



Title of Project : Development Mechanism and Physiological Roles of Brown Fat Regulating Energy Expenditure

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Research Area : Agriculture

Keyword : Food function, Metabolic physiology, Nutritional biochemistry

【Purpose and Background of the Research】

White adipocyte configures body fat, while brown adipocyte (brown fat) is the only cell in the human body engaged in specialized in heat production (Fig). Brown fat, which actively consume fat (triglyceride). Brown fat loss and depression have been shown to cause lifestyle-related diseases such as obesity and diabetes associated with it.

In order to clarify the differentiation mechanism and physiological role of histological distinct brown fat depots, the present study exploits developmental engineering techniques, fluorescence and magnetic resonance (MRI) detection techniques at the level of whole animals. And a novel cell base technique system has been designed to analyze the detailed differentiation molecular mechanism using pluripotent stem cells of human origin. The aim is to help improve the prevention of obesity related diseases such as diabetes and metabolic syndrome.

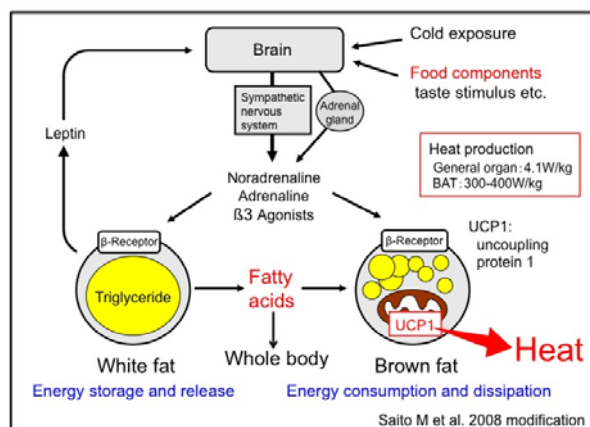


Fig. Shema of Heat production in brown fat

【Research Methods】

In this study, we develop the research results of previous representatives, analyzed at the cellular level and an individual development mechanism occurs in the different type of brown adipose tissues capable of producing heat.

Therefore, we have investigated (1) the preparation of transgenic mice expressing brown fat-specific reporter gene with fluorescent protein, (2) the transgenic mice expressing brown

fat-specific reporter gene with lysine rich protein, and (3) fluorescence and MRI techniques for novel imaging detection in whole animal to promote the development of functional evaluation of brown fat, (4) clarification of the molecular mechanism of brown fat differentiation by using the world's first human brown adipose cell lines.

【Expected Research Achievements and Scientific Significance】

The differentiation mechanism and physiological roles of white fat have already accumulated a lot of knowledge. However, on the brown fat, there are many questions about the mechanisms determining the difference between white fat and brown fat.

We have found the brown fat inducing factors more than 15 years ago. The first result expected in this study is to be able analyze the mechanism of brown fat inducing factor in the whole animal level by a high-resolution techniques. On the second result, brown fat cells by human pluripotent stem cells can elucidate the detailed molecular mechanisms of brown fat differentiation.

By contributing to elucidation of differentiation mechanism and physiological roles of brown fat, this study will promote the development of novel therapies for obesity-related common diseases such as diabetes, metabolic syndrome.

【Publications Relevant to the Project】

- Obesity and fat energy metabolism : Strategy to metabolic syndrome (Kawada, T, Saito M, Ogawa T. eds) Kenpakusha Co. 2008
- Nagase I, Yoshida T, Kumamoto K, Umekawa T, Sakane N, Nikami H, Kawada T, Saito M. Expression of uncoupling protein in skeletal muscle and white fat of obese mice treated with thermogenic beta 3-adrenergic agonist. *J Clin Invest.* 97:2898-2904 (1994)

【Term of Project】 FY2010-2014

【Budget Allocation】 151, 600 Thousand Yen

【Homepage Address and Other Contact Information】

<http://www.foodfunc.kais.kyoto-u.ac.jp>