**Final Report for the Twenty-fourth (2017) Research Grant from Mizutani Foundation for Glycoscience**


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Title of the Proposed Project :

Molecular basis of brown fat development and function by glycosylation


Abstract of the proposed project :

Obesity develops when energy intake chronically exceeds total energy expenditure. Adipose tissue serves as a central regulator of energy balance; white adipose tissue (WAT) functions mainly in the storage of excess energy, whereas brown adipose tissue (BAT) dissipates energy in the form of heat and functions as a defense against hypothermia and obesity. Recent studies identified a “recruitable” form of thermogenic adipocytes, termed beige adipocytes that emerge within subcutaneous WAT in response to certain external cues, such as chronic cold exposure and exercise, often referred to as the “browning” of white fat. Importantly, our recent studies, along with others, indicate that adult human BAT is primarily composed of the recruitable beige adipocytes. Because of its inducible nature and the relevance to adult humans, beige adipocytes have recently attracted much attention as a new therapeutic target for obesity and obesity-related metabolic diseases, such as type 2 diabetes. To further explore the biological roles of human beige adipocytes, we recently identified secretory molecules from human beige adipocytes, so-called “batokine”, many of which are highly glycosylated. Of particular interest, our preliminary study suggests that a batokine, sCNTFRα, has N-linked glycosylation, indicating that beige adipocyte-selective glycosylation is critical for the function of sCNTFRα in the regulation of beige adipocyte development and glucose homeostasis. To test the hypothesis, we aim to characterize the function of sCNTFRα in whole-body energy homeostasis. We further aim to determine the global glycan repertoire of human batokines.