

【Grant-in-Aid for Scientific Research(S)】

Biological Sciences (Medicine, dentistry, and pharmacy II)



Title of Project : Elucidation of pancreatic β -cell function by metabolomics and its clinical application

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Research Area : Diabetes

Keyword : Insulin secretion, Metabolome

【Purpose and Background of the Research】

Glucose and lipid metabolism in pancreatic β -cells play an important role in β -cell function. However, metabolic signals derived from glucose and lipid metabolism involved in insulin secretion, β -cell differentiation and regeneration, and pathogenesis and pathophysiology of diabetes remain largely unknown.

In this study, we aim to elucidate by metabolomics-based analyses:

- (1) **metabolic signals involved in insulin secretion**
- (2) **metabolic signals involved in β -cell differentiation and regeneration**
- (3) **metabolic signal-derived biomarkers for diabetes**

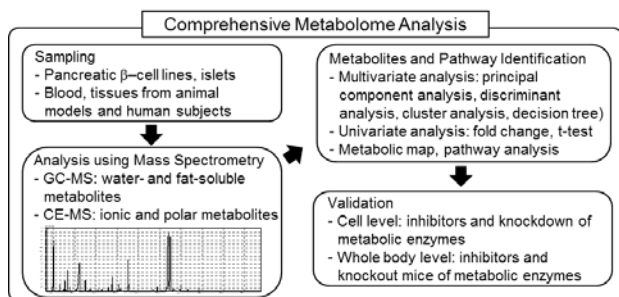
【Research Methods】

- (1) **Elucidation of metabolic signals involved in insulin secretion**

We will identify novel metabolic signals involved in insulin secretion by comprehensive metabolome analysis using pancreatic β -cell lines. We will clarify the roles of metabolic signals at cell, islet, and whole-body levels.

- (2) **Elucidation of metabolic signals involved in β -cell differentiation and regeneration**

We will perform comprehensive metabolome analysis on the mouse model enabling β -cell tracing to clarify the role of metabolic signals in β -cell differentiation and regeneration.



- (3) **Identification of metabolic signal-derived biomarkers for diabetes**

We will perform comprehensive metabolome analyses of human samples (diabetes, impaired glucose tolerance, and normal controls) as well as

animal models, and identify novel biomarkers for diabetes derived from metabolic signals.

【Expected Research Achievements and Scientific Significance】

In specific aim (1), novel metabolic signals regulating insulin secretion and interaction among the signals identified will be clarified, which will greatly enhance our understanding of mechanisms of insulin secretion and identify new therapeutic targets of diabetes. In specific aim (2), metabolic signals involved in β -cell differentiation and regeneration will be identified, which will contribute to establishment of the basis for β -cell replacement therapy for diabetes as well as clarification of the role of cell metabolism in β -cell differentiation and regeneration. In specific aim (3), novel biomarkers for impaired glucose intolerance (IGT) and diabetes before the blood glucose level rises will be identified, which will establish prediction markers of the development of diabetes and contribute to primary intervention for the disease. The present study will provide great insight into biological science and clinical practice.

【Publications Relevant to the Project】

- Seino S, Shibasaki T, Minami K. Dynamics of insulin secretion and the clinical implications for obesity and diabetes. **J Clin Invest** 121:2118-2125, 2011
- Zhang CL, Katoh M, Shibasaki T, Minami K, Sunaga Y, Takahashi H, Yokoi N, Iwasaki M, Miki T, Seino S. The cAMP sensor Epac2 is a direct target of antidiabetic sulfonylurea drugs. **Science** 325:607-610, 2009

【Term of Project】 FY2012-2016

【Budget Allocation】 167,600 Thousand Yen

【Homepage Address and Other Contact Information】

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