

An integrative elucidation of the energy metabolism-regulating system and its disruption

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【Outline of survey】

Glycemic, lipid and energy metabolism represents a critically important process in life's manifestations, where insulin (Ins) and adiponectin (Ad) account for two major pathways for this metabolic process. An integrative conceptualization of the energy metabolism-regulating system and its disruption will hold the key to unraveling the causes of diabetes and the metabolic syndrome (MS) as well as to developing therapeutic modalities for these conditions. The proposed research therefore intends to draw fully on the resources of tissue-specific Ad receptor (AdipoR)-deficient mice for elucidation of the action of Ad in relevant tissues (**Nature** 2003;423:762, **Nat Med** 2006;3:247) as well as on tissue-specific Ins receptor substrate (IRS)-deficient mice for evaluating the effect of primary depletion of Ins action on relevant tissues (**Nature** 1994;372:72, **J Clin Invest** 2004;114:917) to set out to (1) elucidate the mechanisms of interorgan cross-talk in metabolic regulation; and (2) to unravel the mechanisms of cellular function and homeostasis in place in metabolic regulation, thus aiming to give a full picture of the action of Ins and Ad in central and peripheral tissues as well as in the whole body.

【Expected results】

Ours is the only laboratory in the world to have access to and draw on the resources of tissue-specific Ad receptor (AdipoR)-deficient mice for elucidation of the action of Ad in relevant tissues (**Nature** 2003;423:762, **Nat Med** 2006;3:247) as well as on tissue-specific Ins receptor substrate (IRS)-deficient mice for evaluating the effect of primary depletion of Ins action on relevant tissues (**Nature** 1994;372:72, , **J Clin Invest** 2004;114:917) and thus is capable of integrative elucidation of the energy metabolism-regulating system. The proposed research is therefore expected to mark a milestone in that all resulting findings and insights will translate into novel therapeutic modalities for diabetes, the metabolic syndrome and associated cardiovascular disease.

【References by the principal researcher】

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【Term of project】 FY2008– 2012

【Budget allocation】

174,800,000 yen (direct cost)

【Homepage address】

None