Title of Project : Molecular Basis and Disorders of Control of Appetite and Fat Accumulation

Term of Project : FY2010-2014

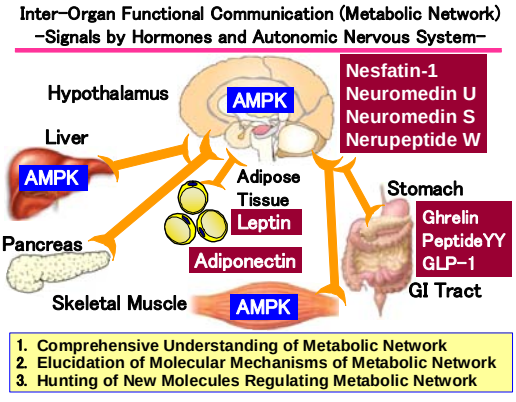
Kenji Kangawa
(National Cerebral and Cardiovascular Center Research Institute, Director General)

【Purpose of the Research Project】

Excess storage of fat in adipose tissue (i.e. obesity) is accompanied by ectopic lipid deposition in nonadipose tissues, such as the liver, skeletal muscles and pancreas. The negative effects of ectopic lipid deposition on glucose metabolism have been proposed to reflect a state of 'lipotoxicity', in which leptin is implicated as an antilipotoxic hormone. Over the past decade, evidence has accumulated that the adipose tissue has multiple functions in both normal physiology and disease. These functions are affected by changes in the adipose-tissue mass and/or the distribution of fat in subcutaneous and visceral adipose tissues. These changes result in dynamic alteration of adipokine production that reflect the severityof obesity, chronic inflammation with the infiltration of macrophages, leptin resistance, and altered autonomic nervous function, in addition to insulin resistance and lipotoxicity. I, therefore, propose the term 'adipotoxicity' to describe the negative effects associated with obesity. Adipotoxicity can be defined as the sum of the negative effects associated with storage of excess fat in adipose tissue on obesity-related clinical features, such as diabetes mellitus and arteriosclerosis. As a consequence, the metabolic syndrome—an obesity-related cluster of diabetes mellitus, dyslipidemia and hypertension — should be studied from a comprehensive viewpoint that is based on the concept of adipotoxicity.

【Content of the Research Project】

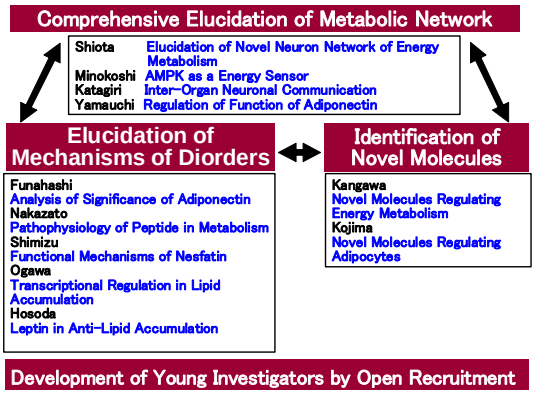
Detailed comparisons of obesity and generalized lipodystrophy (i.e. lack of adipose tissue) have contributed substantially to our understanding of adipotoxicity.



In particular, the dramatic effects of leptin-replacement therapy on patients with lipodystrophy disclosed subtle functions of the adipose tissue, and became the paradigm used to elucidate the mechanisms of adipotoxicity. We should, however, remember that our current understanding of the function of adipose tissue is far from complete.

【Expected Research Achievements】

Further studies on adipotoxicity will hopefully provide a new strategy that we can exploit to prevent and treat obesity and the metabolic syndrome. A key aim of the study of obesity is to understand the significance of the storage of excess fat in the adipose tissue. It is appropriate, then, to coin the term 'adipo-science' to describe studies that aim to evaluate the relationship between adipogenesis and obesity. The definition of adiposcience might also be extended to cover other aspects of metabolism, from appetite regulation to energy expenditure, as well as their mechanisms of action on the adipose tissue.



【Key Words】

Energy Metabolism: Energy metabolism consists of energy intake and energy consumption. There is molecular mechanism in body which regulates energy metabolism. The disorders of energy metabolism causes obesity and emaciation.

Fat Accumulation: There is molecular mechanism controlling fat accumulation in adipocytes and non-adipocytes. Excess accumulation of fat in adipose tissue is defined as obesity while insufficient accumulation is called emation. Excess accumulation of fat in non-adipose tissue causes functional abnormalities which is called lipotoxicity while that in adipose tissue induces functional abnormalities which is called adipotoxicity.

【Homepage Address】

http://www.kuhp.kyoto-u.ac.jp/~med2/jpn/appetite-fat/index.html