The genetic epidemiology of cerebrovascular diseases with high risk genetic factors to establish the secondary prevention program targeting high risk subjects

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【Outline of survey】

Rapture of intracranial aneurysms (IA) and arteriovenous malformation (AVM) result in subarachnoid hemorrhage, which accounts for 2% of the total annual morality in Japan. Especially, IA has attracted the attention of the public because its rapture is triggered by work-related stress. The incidence of Moyamoya is 3 people per 100,000 person years in Japan and often causes stroke in childhood and in the early part of the life. It is already firmly established that genetic factors play pivotal roles in these diseases. However, their mechanisms remain unknown. Apart from genetic factors, it is speculated that anatomical and physiological properties of the cerebrovascular system are associated with their pathogenesis. Epidemiological data has demonstrated that incidences of these three diseases are much higher than in other European countries. For IA, we will search candidate genes in three chromosomal regions: Chromosomes 17, 19, and X, with which we had found significant linkages of IA in pedigrees with IA. For Moyamoya disease, we will conduct positional cloning of the responsible genes on the basis of a pedigree based linkage analysis. For AVM, we will conduct genome-wide association studies by case-control design in isolated populations. On the basis of this research, we will establish a screening program to find subjects at high risk and for them we will be able to provide a program of secondary prevention.

【Expected results】

1) The identification of susceptible genes: we will identify genes which determine susceptibilities for these cerebrovascular diseases.
2) The association of pathological mechanisms with genetic abnormalities to link disease phenotypes: Biological processes that bridge genetic polymorphisms to disease phenotypes will be elucidated.
3) To establish preventive strategies for three diseases: We will develop a screening program to find subjects at high risk. We will also establish the secondary prevention program to provide an early clinical intervention with minimal complications for these high risk subjects. For IA, special emphasis will be put on interactions between genetic factors and on life styles. This will provide supportive evidence for intervention on lifestyle.

【References by the principal researcher】

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【Term of project】 FY 2005 - 2009 | **【Budget allocation】** 67,300,000 yen

【Homepage address】 http://130.54.180.142/index.htm#home