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

Integrated Science and Innovative Science (Comprehensive fields)

Title of Project：Genetic studies on unique phenotypes in MSM/Ms mouse strain

Kenichi Yamamura
(Kumamoto University, Institute of Resource Development and Analysis, Professor)

Research Area：Comprehensice field

Keyword：Disease models

【Purpose and Background of the Research】

Japanese wild mice, MSM and JF1, established by Moriwaki et al. belong to Mus musculus molossinus. We established ES cell lines from MSM with high germline transmission rate. In addition, we developed the exchangeable gene targeting method in which the mouse endogenous gene can be replaced with a human homologue. Using techniques, we will carry out genetic studies on high spontaneous activity, susceptibility to induced pancreatitis, and resistance to diabetes.

【Research Methods】

1. High spontaneous activity

By making chimeric mice composed of MSM ES cells and blastocysts with fluorescence marker (Fig. 1), we will analyze the relationship between localization of ES derived nerve cell and high spontaneous activity and identify genes involved in this phenotype.

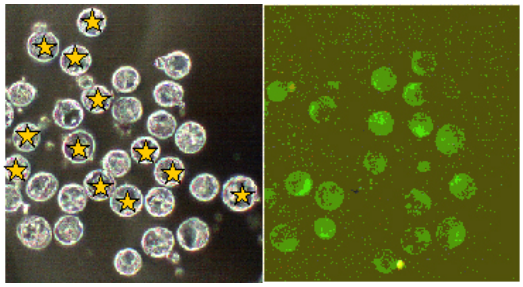

Fig. 1 Blastocysts labeled with fluorescence

2. Susceptibility to cerulein-induced pancreatitis

MSM is susceptible, but C57BL/6 is resistant to cerulein-induced pancreatitis (Fig. 2). We showed that this susceptibility/resistance was determined by regulation of gene expression. Focusing the genes involved in pacreatitis, we will analyze whether the replacement of upstream region confers disease susceptibility.

3. Susceptibility to diabetes

In human, genes involved in maturity onset of diabetes in the young (MODY) were identified. By introducing the same mutation found in human patients, we will analyze whether diabetes develop in MSM or B6 mice.

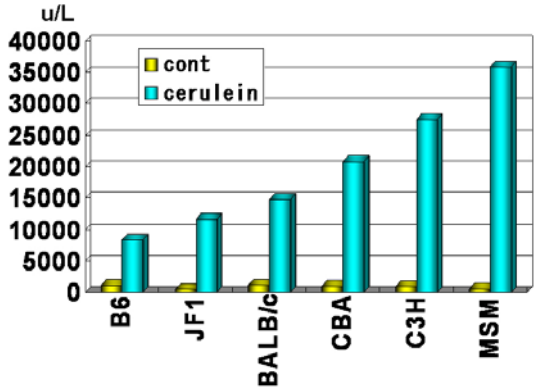

Fig. 2 Susceptibility to pancreatitis

【Expected Research Achievements and Scientific Significance】

Using MSM strain, we will be able to find new genes involved phenotypes, to find new function of genes, to find the relationship between phenotype and regulation of gene expression. In addition, knockout mice or gene replaced mice developed here will be deposited to the Center for Animal Resources and Development as a resource for scientific research.

【Publications Relevant to the Project】

・Araki, K., Takeda, T., Yoshiki, A., Obata, Y., Nakagata, N., Shiroishi, T., Moriwaki, K. and Yamamura K. Establishment of germline-competent embryonic stem cell lines from the MSM/Ms strain. Mammal. Genome 20: 14-20, 2009.

・Ohmuraya, M. and Yamamura, K. Autophagy and acute pancreatitis: A novel autophagy theory for trypsinogen activation. Autophagy 4: 1060-1062, 2008.

【Term of Project】 FY2009-2013

【Budget Allocation】 162,000 Thousand Yen

【Homepage Address and Other Contact Information】

http:// www.irda.kumamoto-u.ac.jp/