【Grant-in-Aid for Scientific Research(S)】
Biological Sciences (Medicine, dentistry, and pharmacy Ⅱ)

Title of Project : Study on the relationship between multiple sclerosis and gut microbiome

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Research Area : Medicine, dentistry, and pharmacy
Keyword : Neuroimmunopathology

【Purpose and Background of the Research】

The purpose of this study is to test the hypothesis that multiple sclerosis (MS) pathogenesis may involve alteration of gut microbiome due to the change of life style. In Japan there was only 1000 registered patients with MS 30 years ago. But since then the patient number has greatly increased, and now reaches over 15,000. In Japan, an increase of inflammatory bowel diseases is also apparent, which is suspected to result from dysbiosis of gut flora. We have reported that altering gut flora significantly reduces the severity of experimental autoimmune encephalomyelitis (EAE), a rodent model for MS, in parallel with reducing Th17 cells (Yokote et al. Am J Pathol 2008).

【Research Methods】

We here examine the microbiome in the feces of MS and healthy subjects by using the gene sequence-based analysis of 16S rRNA and bacterial metagenome. In parallel, we analyze clinical profiles of the patients

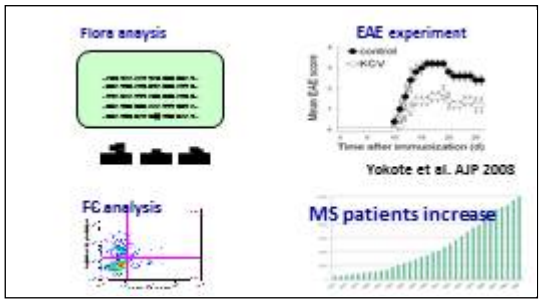

Figure 1

and immunological parameters by using flow cytometry. After we identify bacterial species that are greatly reduced or increased in the feces of MS, we will transfer the bacteria in germ-free mice and ask whether the gnotobiotic mice may represent immunological abnormalities that are relevant to the prevention or augmentation of MS.

【Expected Research Achievements and Scientific Significance】

Recent works have firmly established that gut flora is critically involved in the development of autoimmune diseases in rodents. However, it is not clear if the observations have relevance to understanding much more complex human pathogenesis. This project is primarily planned for identifying alterations of gut microbiome in MS. Owing to the power of gene-sequencing analysis, we are assured that our primary aim will be fulfilled and we may be able to identify bacterium, which plays a key role in MS or in healthy status.

Our results should also have implications for understanding the mutual relationship between human immune system and commensal flora.

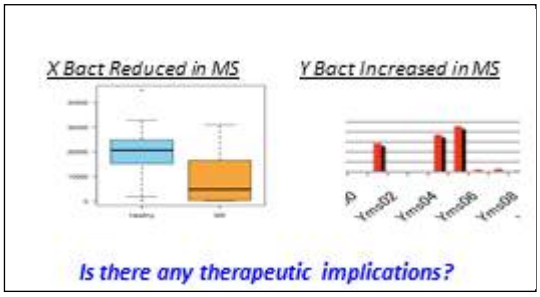

Figure 2

【Publications Relevant to the Project】

Yokote H et al.: NKT cell-dependent amelioration of a mouse model of multiple sclerosis by altering gut flora. ***Am J Pathol*** 173: 1714-1723, 2008

Miyazaki Y et al. : Mucosal-associated invariant T cells regulate T helper type 1 response in multiple sclerosis. ***Int. Immunol.*** 23:332-337, 2011

【Term of Project】 FY2012-2015

【Budget Allocation】 112,400 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.ncnp.go.jp/nin/guide/r_men/index.html