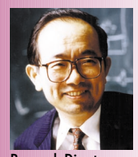
CHIBA

Established in FY2001

Development of New Technologies Based on Genome Information

Project Director
Tsugio Kimijima
Coordinator for new business development
Chiba Industry Advancement Center



Research Director
Michio Oishi
Director
Kazusa DNA Research Institute

Technology Facilitator
Noboru Tomioka
Senior Chief Researcher
Kazusa DNA Research Institute

R&D Targets

Chiba prefecture is conducting research projects into advanced technologies for the post-genome era that are based on the genetic resources and associated technologies that have been accumulated at the Kazusa DNA Research Institute. With the aid of such projects, we aim to create a regional Center of Excellence (COE) specializing in biotechnology by developing new technologies and products in the medical field.

Background

Chiba prefecture is promoting the development of new regional industries by assembling biotechnology related research functions at the Kazusa Academia Park. As part of this development, we will establish the core laboratory at the Kazusa DNA Research Institute, which is located in the park. Our aim is to promote the development of new technologies, innovative products and to contribute to the development of the new biotech industries in collaboration with regional businesses, public research institutions and the universities.

R&D Themes and Organizations

1. Obtaining Long Mouse cDNAs, Analyzing their Structures, and Developing Technologies for Cloning and the Analysis of long cDNAs with High Efficiency

This project aims to acquire 2,000 types of long mouse cDNAs that correspond to the long human cDNAs, which have been accumulated at the Kazusa DNA Research Institute. The laboratory strains of the mouse have been used most frequently in the research area of mammalian biology or medical science as a model animal. Genetically modified mice by using mouse long cDNA will contribute in research for the development of pharmaceuticals. We will construct several sets of gene mouse bank consisting of long cDNAs (>4,000 bp) that are not easily obtained.

(Kazusa DNA Research Institute, Institute of Research and Innovation, Chiba University)

2. Development of Technologies for the Production of Antibodies Against Proteins Encoded by the Long Mouse cDNAs, their Production and Evaluation

We will establish reliable technologies for the efficient production of a large number of antibodies and produce more than several hundreds of the antibodies that can be applied for practical use.

(Kazusa DNA Research Institute, Protein Express Co., Ltd., Institute of Research and Innovation, National Center of Neurology and Psychiatry, Japan)

3. Development of Technologies for the Production of DNA and Antibody Array and their Production and Evaluation

In this theme, we will aim to achieve the following. 1) The establishment of technologies for the immobilization of DNAs or antibodies. 2) Development of microarrays with 2,000 different cDNAs or antibodies. 3) Improvements to a microarray spotter and assemble of an array detector with a high sensitivity. By using these microarrays and equipments, we will analyze long mouse cDNAs(mKIAA clones), the most of their functions being as yet known.

(Kazusa DNA Research Institute, Kaken Geneqs, Inc., Fuji Photo Film Co., Ltd., Chiba University, Tokyo University of Science, University of Tokyo, Tokyo Institute of Psychiatry)

4. Construction and Management of a Database for all of the Joint Research Projects

We will construct a relational database which includes the general databases covering our mouse long cDNA clones, antibodies and microarrays. The mouse relational database will be systematically linked with the database of the human long cDNAs (KIAA clones) in the Kazusa DNA Research Institute.

(Kazusa DNA Research Institute, NS Solutions Co., Ltd., Mathematical Systems, Inc.)

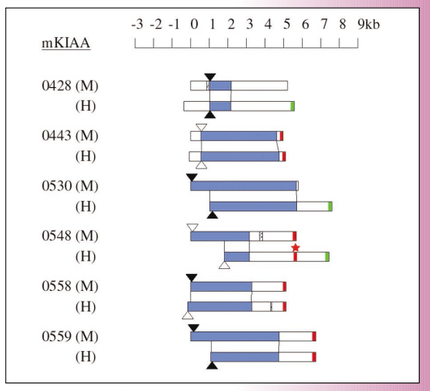
For details, please refer to our Website. (http://www.ccjc-net.or.jp/~create/)

- Central Project Organization
  Chiba Industry Advancement Center
- Administrative Departments in Charge
  Industrial Promotion Division, Commerce, Industry and Labor Department, Chiba Prefecture
- Core Laboratory
  Kazusa DNA Research Institute

Primary R&D Achievements

1 Development of Efficient Long Mouse cDNA Cloning Technology, and Determination of the Entire Sequences (R&D Theme 1)

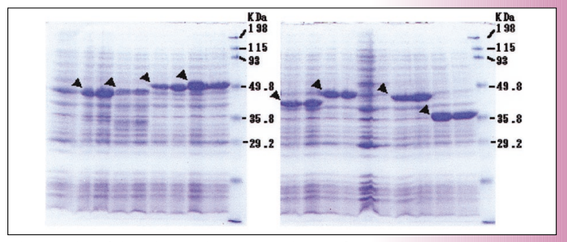
The Kazusa DNA Research Institute has been accumulating human libraries of long cDNA (>4,000 bp). The reason for this strategy is that we believe the functions of biological phenomena in diseases such as cancers, brain diseases and life-style related diseases might be clarified in terms of the expression of genes that code for large proteins. So far in this project, we have achieved the following. 1) The Development of an efficient method of cloning the genes of mice, which are homologous to human genes. 2) The Screening of about 130,000 clones in the mouse cDNA libraries constructed with long cDNAs derived from the brain and other organs. 3) Beginning to obtain the targeted mouse 2,000 long cDNAs, the selection was completed and the 1,750 candidates were picked up for the next sequencing step. 4) Completion of the entire sequencing of approximately 900 clones. 5) For 500 of all the 900 clones, the related information of entirely sequenced is available on the World Wide Web at http://www.kazusa.or.jp/rouge.



Comparison of the structures of mouse (M) and human (H) long cDNAs (The blue boxes indicate the protein coding regions)

2 High Throughput Recombinant Antigen Preparation Technologies (R&D Theme 2)

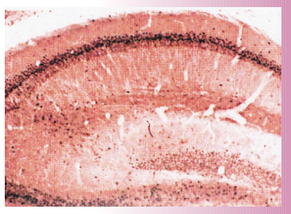
In order to improve the efficient production of a large number of antibodies, we have first developed the requisite technology for the high throughput preparation of antigen proteins. Specifically, we have developed a new *in vitro* homologous recombination method that is capable of processing simultaneously the reactions of 96 samples. (Conventional methods restricted the processing of only one reaction sample at a time.) We have also developed technologies for expressing and purifying recombinant proteins with high efficiency. The recombinant proteins obtained by this method are confirmed to be advantageous for the preparation of antibodies.



The results of the electrophoretic analyses of recombinant proteins expressed in E.coli

3 Analysis of Specific Protein Expression Patterns Using an Immunohistochemical Staining Method (R&D Theme 2)

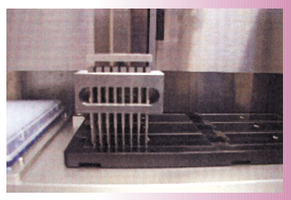
In this theme, we have analyzed specific localization of the antigens in the mouse brain, using an improved immunohistochemical method. As a result of the analyses of about 100 antibodies, it has been confirmed that specific or characteristic immunohistochemical stains for 90% of the antibodies can be obtained from various regions of the brain.



In this case, specific localization of the antigen in the hippocampus region of mouse brain was observed.

4 Development of an Improved DNA Arrayer (R&D Theme 3)

In order to conduct high-density microarrays of the DNAs obtained in R&D Theme 1 or antibodies prepared in R&D Theme 2, it is necessary to develop an improved and reliable array spotting system. The improved arrayer system is capable of spotting at twice the speed and with a higher accuracy than has been possible with our previous system.



An improved DNA arrayer

5 Construction of a Consistent Process Management System for the Shotgun Sequencing of Mouse Long cDNAs and the Preparation of Antibodies (R&D Theme 4)

To help increase the throughput of analyses of cDNA sequences and the preparation of antigens, we have built a database with a process management application that is potentially useful for identifying the status of all the required experimental processes.