Tokai J Exp Clin Med., Vol. 23, No. 2, pp.95-96, 1998

Malaria Genome Project in Japan

Jun-ichi WATANABE, Mihoko IMADA, Yutaka SUZUKI*, Zenei SASAKI*, Hiroko HATA*, Junko MIZUSHIMA-SUGANO*, Sumio SUGANO*, Hideo IKEDA**, Kosuke TASHIRO*** and Somei KOJIMA

Department of Parasitology,
**Department of Virology,*
***Department of Molecular Biology, Institute of Medical Science, The University of Tokyo, Tokyo Japan*
****Molecular Gene Technics, Graduate School of Genetic Resources Technology, Kyushu University, Fukuoka, Japan*

Malaria genome project, an effort to determine all the nucleotide sequences of plasmouim has well started by several groups of malariologists in the world. With a modest genome size, *i. e.*, 3×10^7 base pairs divided in 14 chromosomes, *Plasmodium falciparum* is a good target because of its medical importance. Recently, it was announced that two institutes, Sanger Centre and TIGR which were involved in sequencing human genome had decided to participate in malaria genome project. Since 1990 we have studied the structure of the chromosome #4 on which DHFR-TS (dihydroforate reductase-thymidine synthase) enzyme is located and established the high resolution physical map (1). Extending this we have launched Malaria Genome Project in Japan.

Our strategy

1) For genomic DNA sequencing, we are preparing genomic libraries constructed with P1 phage. It is a single copy phage which can harbor a 100kb insert in *E. coli*. With the genome notoriously rich in AT, the high frequency of recombination has hampered previous efforts. Lack of intermolecular recombination between phage DNAs is of advantage in this system.

2) To further focus on stabilization of malaria DNA, which should be critical in this genome project, we are selecting *E. coli* mutant strains which, having disruption of the genes involved in recombination of the host genes, can maintain malaria DNA stable. Relevant strains should be of use not only for malaria genome study but also for that of various organisms.

3) Genomic DNA data should be supplemented with information about the expression of the genes. Using a method we have established to clone a full length mRNA (2), a cDNA library was produced from erythrocytic stage *P. falciparum*. Preliminary sequencing revealed that most of the 10^5 clones contained AT rich malaria sequences, some of which corresponded to presumable full length mRNAs.

Prospect

As projects 1 and 2 are being in progress, we are optimistic about the construction of a stable library. With the average insert size of 100 kb, each chromosome can be covered by scores of clones. High resolution map of Chr #4 and specific probes with known localization (1) will help rapidly organize clones. Versatility and feasibility of P1 phage is expected to replace YAC library which is now in wide use.

Uniqueness of the malaria genome is duplication of genes which is closely related with adaptation to two hosts, mosquito and human. Actually, three different genes for rRNA are used sequentially in parasite in different stages. Conserved morphological structures in each host should be controlled by related genes. Thus, comparisons of duplicated genes is expected to elucidate the mechanism of parasitism and adaptation to hosts.

Finally, characterization of expressed mRNA sequences from different stages of parasites is essential to complement analysis

Jun-ichi WATANABE, Department of Parasitology, Institute of Medical Sciense, University of Tokyo, Shiroganedai 4-6-1, Minato-ku, Tokyo 108-0071, Japan, e-mail; jwatanab@hgc.ims.u-tokyo.ac.jp

of genomic DNAs for the understanding of the functions of the numerous genes. Moreover, expression system of full length mRNA clones, which is now available, should enable the screening of vaccine candidates for the first time.

REFERENCES

1) Establishing a physical map of chromosome No.4 of *Plasmodium falciparum*. Junichi Watanabe and Joseph Inselburg *Mol. Biochem. Parasitol.* 65 189-200, 1994

2) Construction and characterization of a full length-enriched and a 5'-end-enriched cDNA library. Yutaka Suzuki, Kiyomi Yoshitomo, Kazuo Maruyama, Akira Suyama and Sumio Sugano *Gene* (submitted)

Supported by Grants-in-Aid for Scientific Research on Priority Areas (08281101 & 08281103).