Genomics in Japan

It is widely acknowledged that Japan lags behind the USA and Europe regarding genomic research. The Japanese government is fully aware of the economic importance and opportunities of the functional genomics business and directs substantial funding into this field. The total annual spending of the Japanese government towards genomic research is estimated in the order of JPY 30–40 billion.

Japanese government assists

Although the overall government budget for the current fiscal year is very tight, funding for genome-related research projects has doubled. For example, in August, a genome-informatics project (budget JPY 1.5 billion) and a project establishing a patent database for DNA-sequences (budget JPY 183 million) will commence under the guidance of the Ministry of International Trade and Industry. The recent approval by the Science and Technology Agency to construct a Biomolecular Research Center, in close co-operation with the Institute of Physical and Chemical Research (RIKEN), underlines how seriously the Japanese government views the situation. The details of the 15-year programme have yet to be fully established, but the core will be the analysis of the human chromosome 21 (in collaboration with the University of Tokyo) and the structure–function analysis of proteins (proteomics). In the first five years, a budget of JPY 50 billion has been allocated, and some 200 researchers are expected to work in the different projects. This programme is a strategic expansion of the current activities of the Human Genome Sequencing team in Japan, who contribute to the worldwide Human Genome Project. It consists of four contributors:

- Kitasato University (focusing on chromosome 21; ~6000 kbp sequenced).
- Keio University (chromosome 21 and 22; ~4500 kbp sequenced).
- Tokai University (chromosome 6; ~2000 kbp sequenced).
- Japanese Foundation for Cancer Research (focusing on chromosomes 3, 8 and 9; ~5000 kbp sequenced).

At the National Institute of Genetics (Mishima), the DNA Data Bank of Japan (DDBJ) is located; this centre coordinates its research with GenBank (USA) and EMBL/EBI (Europe).

Other large-scale projects and consortia

In recent years some other consortia or large-scale projects have been established. Remarkably, most of these are under the guidance of one or other of the ministries of the Japanese government. In March 1996, Genox Research was established with the financial support of the Ministry of Health and Welfare. In this company, eight major Japanese companies (Eisai, Kyowa Hakko, Sankyo, Tanabe Seiyaku, Kirin Brewery, Yamanouchi Pharmaceutical, Olympus and Hamamatsu Photonics) are co-operating, together with national universities, to create a genomic database for allergy related diseases such as allergic rhinitis, asthma and atopic dermatitis. The expression profiles of patients' white blood cells are being analyzed and a unique database that combines a gene expression database with a clinical information database is being constructed.

In March 1996, the Helix Research Institute (HRI) was established by the Japan Key Technology Center with ten private companies to develop effective technologies for identifying new biologically important genes and to characterize their function. In this six-year project, 70% of the costs will be indirectly paid by the Ministry of International Trade and Industry and 30% by the participating companies: Chugai Pharmaceutical, Fujisawa Pharmaceutical, Hitachi, Kyowa Hakko, Mitsubishi Chemical, Sumitomo Chemical, Taisho Pharmaceutical, Yamanouchi Pharmaceutical, Yoshitomi Pharmaceutical and a financial company. HRI accommodates three major laboratories (genomics, bioinformatics and biological technology) with nearly 50 research staff. In co-operation with the University of Tokyo, HRI has constructed libraries with enhanced representation of full-length clones using an oligo-capping method; full-length sequencing has begun using these libraries. Construction of mouse full-length cDNA libraries is also performed at the University of Tokyo.

Vector technology for gene therapy

The project DNAVEC commenced in March 1995. This work is focused on the research and development of 'vectors', which form the fundamental technology for gene therapy. DNAVEC is a seven-year national undertaking, in which 50% of the capital has been indirectly provided by the Ministry of Health and Welfare. Seven private companies (Hisamitsu Pharmaceutical, Kyowa Hakko, Sankyo, Shionogi, Sumitomo Pharmaceuticals, Tanabe Seiyaku and Yamanouchi Pharmaceutical) have invested in DNAVEC to cover the rest of the JPY 4.5 billion capital and to involve their research personnel.

Kazusa DNA Research Institute

The Kazusa DNA Research Institute (KDRI) was established in October 1994 by the Chiba Prefecture Government and was approved as a non-profit organization by the Ministry of International Trade and Industry and the Science and Technology Agency. The annual budget of KDRI, located in the Kazusa Academy Park, is about JPY 1.8 billion. The institute houses about 25 scientists and 50 supporting staff. Some of KDRI's projects include:

- Sequencing of the 3.6 Mb genome of a cyanobacterium (photosynthetic bacterium), completed in March 1996.

  1359-6446/98/$19.00. PII: S1359-6446(98)01229-X

- Sequencing of full-length cDNAs from cultured human cells (including brain) with a capacity of 2 Mb of cDNA sequence per year (representing ~350 cDNA clones).
- The development of new technologies, particularly for large-scale DNA sequencing.

The Kazusa Academy Park is seeking to create a so-called 'DNA valley' in Chiba. Recently, Tokyo Tanabe Seiyaku and Sato Pharmaceutical announced intensification of their R&D efforts at the complex in the field of DNA informatics to support the development of new antibiotics. The KDRI has decided to actively disclose its accumulated cDNA information to promote its utilization in industrial applications. The idea is to encourage companies to participate in KDRI's ongoing research.

Researching the aging process

The AGENE Research Institute, a company founded in March 1994, focuses on the research of individual and cellular aging. The research period is seven years and a budget of JPY 3.1 billion supports the work of about 20 researchers. Half of the capital is derived indirectly via the Ministry of Health and Welfare and the other half by four companies (Nippon Roche, Eisai, Kissei Pharmaceutical and Meiji Seika). Projects include:

- Cloning and analysis of the functions of Werner's syndrome genes and regulatory genes in cell proliferation to reveal information about aging specific diseases such as cataract, osteoporosis and arteriosclerosis, known to be rapidly expressed in Werner's syndrome.
- The development of assay systems for aging gene expression, which is expected to contribute to the development of new therapeutics against aging-associated diseases.

Recent news

In April 1998, Hiroshi Matsumoto and colleagues at the Nagoya University announced success in creating a miniature artificial chromosome of about one-tenth the size of a human chromosome. This newly created chromosome is stable in human cells, is not lost upon cell division and does not acquire unknown host DNA from human chromosomes; thus, bringing an effective gene therapy one step closer. This knowledge may be implemented in the first gene treatment for breast cancer in Japan, which is currently in development. A team from a hospital belonging to the Foundation of Cancer Research Institute (Tokyo) will utilize new gene-transplant techniques on 10 patients. The technology combines the administration of the anticancer drug docetaxel and the implantation of genes in blood stem cells using a vector. If successful, the technology may also be used for treatment of ovarian cancer, cerebral tumours and child cancers for which anticancer drugs have been found only partially effective.

In May 1998, the GenomeNet announced the installation of a new supercomputer system at their Tokyo center. The GenomeNet is a Japanese network of databases and computational services for genome research and related areas of research in molecular and cellular biology. The GenomeNet was established in 1991 and resides under the auspices of the Ministry of Education, Science, Sports and Culture.

Company activities

There have been several recent developments in corporate research projects. Chugai Pharmaceuticals and Kirin Brewery together with five other non-Japanese companies participate in the DiscoverEase protein development platform of Genetics Institute. Another active Japanese company in the field is Hitachi, sponsors of a three-year project to develop a Genome Knowledge Discovery System at the University of Tokyo. Hitachi have also announced their intention to launch, later in 1998, a new, rapid and highly sensitive capillary-array gel-electrophoresis-based DNA-sequencer on the market that is believed will be able to process 20,000 samples a day.

Yamanouchi Pharmaceuticals plans to start in-house basic genome research in the expectation of developing effective new drugs for treating diseases of the nervous system, inflammatory disorders and other target fields. Also, Mitsubishi Chemical Corporation (MCC) has started nine joint projects, with bioventure businesses and universities outside Japan, to carry out fundamental research on genomics. These tie-ups are within MCC's target R&D sectors – cancer, immunology, CNS, circulatory system and diabetes.

Japan – a world competitor?

Japan is definitely gearing up in trying to become a competitive partner in the genomics business. And although not many Japanese bioventures are visible, which is often ascribed to as a difference in cultural attitude, many enterprises (including those with a non-related core-business) are directing money and exploring research opportunities in the expanding biotechnology market in Japan. This has already attracted the first foreign venture businesses to establish their own sales and marketing base in Japan.

First International Workshop

On 27–28 April 1998, the *First International Workshop on Advanced Genomics: Expression Profiling and Related Technologies* was held in Tokyo. Commemorating the retirement of Professor Kenichi Matsubara (International Institute for Advanced Studies, Kyoto), who was one of the first in the world to stress the importance of cDNA libraries. With over 300 (mostly Japanese) participants, the workshop included eight presentations from Japanese and 24 lectures from mostly American venture businesses. This exemplary workshop highlighted the many activities of current research in Japan. However, with the structural genomics of many large genome organisms (including human) due to be completed in the near future, a dramatic development of functional genomics can be expected. The Second Workshop has already been scheduled: it will be held in April of next year near Tokyo.

Fred Elgersma, BioTransfer Ltd, Tokyo
e-mail: avebio@gol.com