

# JAPAN ROUNDUP

Nobel Prize winner Prof. Tonegawa (Massachusetts Institute of Technology, Cambridge) and emeritus Prof. Watanabe (Keio University), who taught young Tonegawa when he was in Japan, have agreed to act for the next year as scientific advisers to the Chiba Prefectural Government. They will play an active role in the planning of Jousou New Research and Development City—especially for the Jousou Institute for Life Sciences, which will open in 1996 as the core system for the research city. The Institute will be established as a DNA Analysis Center: the staff will consist of 90 research scientists and technicians its first year, with the staff eventually expanding to 300. Prof. Watanabe explained that the new Institute will be the first in Japan for DNA analysis. Prof. Tonegawa suggested that it will be vital to the Institute to attract an international array of scientists.

Prof. Uozumi's group at Tokyo University, Department of Agriculture, has engineered *Klebsiella oxytoca*, a bacterium associated with rice, for improved nitrogen-fixing abilities. Normally, *K. oxytoca* is much poorer at fixing nitrogen than *Rhizobium*, which forms root nodules on beans. Uozumi and his colleagues have spent the last 10 years analyzing *K. oxytoca*'s 20 nitrogen fixation-related genes. From these, they have isolated two major ones—the gene for suppressing nitrogen fixation when ammonia is present in the soil, and the gene for promoting fixation. The group successfully destroyed the suppressor gene, thus enhancing the promoter's function. When they added the engineered microbe to soil, they found that the rice increased in nitrogen content and dry weight by about 30 percent. The nitrogen content of the soil increased also. The engineered microbe is also genetically stable.

Researchers at the National Institute of Agrobiological Resources and Mitsui Toatsu Chemicals (Tokyo) have successfully identified and isolated a rice promoter gene, which regulates the expression of foreign genes. The promoter has 850 base pairs and enhances gene expression 10-fold, specifically in rice leaves. The group expects to develop a new variety that is insect- and herbicide-resistant.

Japan Tobacco (Tokyo) scientists

have developed a cucumber mosaic virus (CMV)-resistant recombinant leaf tobacco from a commercially cultivated variety. It will be the company's first biotechnology product. The foreign gene increases the amount of viral satellite RNA, which mitigates disease symptoms, but does not influence the quality of the tobacco leaf. CMV is one of the most serious diseases in tobacco, as is tobacco mosaic virus, but in contrast to the latter, a CMV-resistant wild variety does not exist. Accordingly, the present approach is expected to become a model system and applicable to other kinds of plants, including tomato.

Plantech Research Institute (Tokyo; a joint research company established by Mitsubishi and Mitsubishi Kasei) researchers have successfully suppressed CMV growth in tobacco, as well. Their method introduces viral antisense RNA into the plants. The antisense RNA blocks the production of 3A protein, which is necessary for viral transmission to the next cell. The scientists combined the antisense RNA with a hygromycin-tolerance marker gene.

The Agency of Industrial Science & Technology's Fermentation Research Institute has discovered a new bacterium which generates methane while decomposing acetic acid. Scientists expect to use the bacterium in an efficient anaerobic water processing reactor system.

The bacterium itself is only two microns in length, but reproduces in a filiform linkage of up to 100 microns, making it easy to retain within the reactor.

Anaerobic water processing reactor systems run at high temperatures—55–60°C. Under these conditions, the rate-limiting factor is bacterial growth rate. The new strain's growth rate is 2–3 times higher than conventional bacteria, resulting in a significant improvement in efficiency.

Researchers at Ajinomoto (Tokyo) have developed a cost-effective suspension and spinner culture system for mass-producing proteins. Using this system, the company successfully obtained a high yield of 10 mg per liter of human blood-derived erythroid differentiation factor (EDF), which is difficult to produce in *E. coli*. The system consists of a serum-free medium, ASF-CHO, and a recombi-

nant Chinese hamster ovary (CHO) cell line. The ASF-CHO medium contains only 60 micrograms per ml (in contrast to 5 mg per ml of serum-containing medium) of miscellaneous proteins and is suited to purify target proteins. Moreover, the researchers found they could grow suspension cultures of CHO cells in serum-free medium containing low concentrations of agar.

Takara Shuzo (Kyoto) scientists, in collaboration with Prof. Yamaguchi at Teikyo University, Research Institute for Medical Mycology, have discovered a new antibiotic—R106—that is effective in treating fungal infections. R106 is a cyclic peptide with a molecular weight of about 1,000. It kills fungi directly rather than suppressing their activity. R106 was effective in mice and its therapeutic index was as high as 100. This safety margin is especially good in contrast to the other anti-fungal therapeutics now on the market.

Mitsubishi Kasei Institute for Life Sciences (Machida) researchers have discovered an activator protein that enables endoglycoceramidase (EGC) to work in a neutral pH environment. EGC cuts glycolipid extensions at cell surfaces, but needs the help of a surface-active agent, Triton X-100. This agent makes the environment acidic (pH 5.0–5.5), causing damage to living cells. The activator protein enables the enzyme to cut 60–70 percent of the glycolipid extensions in a neutral pH environment.

Both EGC and the activator protein were derived from Actinomycetes; there are two subsets of the activator (I and II) which are respectively specific to EGC I and II isozymes.

BIDEC (Bioindustry Development Center) has changed its English name to JBA (Japan Bioindustry Association). The foundation was established in 1987 as the first organization for academic/industrial collaborations in bioindustry. For the past three years, the foundation has played an important role in founding bioindustry in Japan and is now expected to promote international collaborations.

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