JAPAN ROUNDUP

Researchers led by Kyoto University's Kenji Sonomoto have developed a bioreactor capable of producing the blue pigment of lavender flowers continuously for up to three months. The lavender plant cells remain viable for extended periods of time because they are immobilized in a special hydrophilic polyvinyl alcohol resin that is polymerized by exposure to light. Following this relatively gentle polymerization, the immobilized lavender cells are immersed in culture medium supplemented with the amino acid cysteine. Because few blue or purple dyes are suitable for use as food additives, there is considerable demand for the lavender pigment as a food coloring.

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Scientists at Toyo Polymers Inc. (Osaka) have developed a bioreactor that degrades dimethylformamide (DMF), a by-product of the production of synthetic leather, acrylic fabrics, and paints. The core of this new bioreactor contains a resin in which a special strain of aerobic bacterium is immobilized. When contaminated water is passed through the bioreactor, the bacteria convert DMF to carbon dioxide and nitrogen gas, reducing DMF concentrations to 3 percent. Current DMF distillation decontamination techniques are unable to economically reduce DMF concentrations below 10 percent, resulting in DMF-containing fluids being diluted and released directly into the environment. Although small amounts of DMF are not believed to be dangerous, chronic exposure may cause liver damage. Toyo Polymers is in the process of conducting a market survey to determine the demand for the DMF bioreactor.

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Scientists working under the direction of Masashi Omori at Otsuma Women's College have demonstrated that removing the oxygen from tea leaves soon after picking yields a tea that reduces blood pressure in rats with inherited hypertension. The researchers determined that this processing causes the tea leaves to accumulate large amounts of gamma aminobutyric acid (GABA), a neurotransmitter known to lower blood pressure. Because of its high concentration of GABA (pronounced "gyaba" in Japanese), this new tea has been dubbed "gyabalon" tea.

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Morinaga Seika (Tokyo) and Sumitomo Shoji (Tokyo) are joining forces to field-test Morinaga Seika's new fungicide against *Aspergillus flavus* and *A. parasiticus*. These fungi—which grow on peanuts, rice, corn, and other grains—produce the cancer-causing protein aflatoxin. Due to strict regulations in Japan, testing is taking place in Thailand and Australia where aflatoxin contamination of rice and other grains poses an important health threat. The annual market for an effective anti-aflatoxin fungicide is estimated by Japanese sources to be approximately $30–35 million. Assuming the field-tests go well, the companies plan to bring the new fungicide to market in 3–5 years.

Prepared by Hal Plotkin and Ken Coleman, Biotechnology in Japan Newsservice, *Japan Pacific Associates (Palo Alto, CA).*

PROPRIETARY TECHNOLOGY

GENENTECH SCORES BASIC U.S. PLASMID PATENT

WASHINGTON, D.C.—Some eight years after Genentech first filed for proprietary protection to cover the plasmid system it used to produce human insulin in *Escherichia coli*, the U.S. Patent and Trademark Office (PTO) has finally issued a patent. The major question now concerns the breadth of coverage that this potentially basic genetic engineering patent may provide.

Genentech (South San Francisco, CA) plans to "license the patent at reasonable rates on a case-by-case basis"; industry representatives guess that royalties on product sales might run in the one-half to one percent range. As a practical matter, though, a broad consensus of attorneys, financial analysts, and biotechnology executives agree that it is in the industry's best interest that Genentech makes moderate licensing demands—and that users of the technology accept these terms.

The patent's initial claim, which is traditionally the broadest claim, covers "A recombinant DNA cloning vehicle, suited for transformation of a microbial host." According to the patent, this "vehicle" (or vector) consists of two parts: a control region native to the host and a DNA sequence coding for a foreign protein.

Secondary claims specify that the vector is a plasmid; that the promoter-operator system is either the *E. coli* lactose or tryptophan operon; that the host is a bacterium (specifically *E. coli*); and that the gene produces a mammalian hormone (insulin).

"It's certainly a very broad patent, but it does have limitations," says Iver Cooper, a patent attorney with the firm of Mackler, Cooper & Gibbs (Washington, D.C.). "It would not seem to cover work being done in mammalian cells, because it's limited to a microbial host." Neither, he adds, would the patent seem to cover a viral vector, or a plasmid with a control region that came from a different organism than the host. For example, if a promoter from another enterobacterium worked in *E. coli*, one could argue that it did not infringe.

But a patent attorney from a major Genentech competitor does indeed worry about the patent's scope. "I've been asking people how they view the term 'microbial,'" he explains. "Some people say it means bacteria and yeast. But one person said it meant 'microscopic,' which would include mammalian cells."

The new patent can also be viewed from another intriguing angle. Depending on the extent to which a licensee may have to report and itemize its product sales, "the patent would be a tremendous source of information for Genentech," says Robert Benson, a patent lawyer with Leydig, Voit & Mayer (Chicago, IL). Not only might Genentech be privy to an inside look at the financials of its competitors, but the firm might be able to use disclosed information to detect possible infringement of its other patents.

Ironically, the potentially crucial insulin patent issued in more than 20 countries before the U.S. PTO rendered its decision. According to PTO Assistant Secretary and Commissioner Donald Quigg, more than 1,800 applications containing nucleic acid sequence data are now pending—a backlog that PTO is trying to remedy both by hiring more examiners with relevant expertise and by building a computer system to handle such specialized information. PTO plans to standardize its data format so that sequence information in patents is compatible with other electronic systems. **—Norman Bauman**

(with Jeffrey L. Fox and Arthur Klausner)