Japanese react to *ex vivo* gene therapy patent

The recent award of a patent covering all *ex vivo* gene therapy to the US National Institutes of Health (NIH) has caused a stir in Japan and likely will not be recognized under Japan's patent law should the NIH decide to file a patent there.

The patent, issued by the US Patent and Trademark Office in March (*Nature Medicine* **1**, 392; 1995), covers all *ex vivo* gene therapy where human cells are genetically altered in the laboratory to express potentially therapeutic genes and then reintroduced into the patient.

"According to our guidelines, therapeutic means cannot be patented, so Japan will not recognize this patent," says Setsuko Asami, an official at the patent office.

It also seems unlikely that the patent will be enforceable in Japan or elsewhere in Asia — where there is currently great interest in gene therapy research — because the section in the General Agreement on Tariffs and Trade relating to intellectual property rights (section 5, article 27) gives member countries the right to prohibit the patentability of diagnostic, therapeutic and surgical methods used in the treatment of humans or animals.

Japanese officials who are trying to stimulate the development of a homegrown gene therapy industry are concerned about the effect the patent award might have on their plans to reduce Japan's reliance on foreign technology, particularly from the United States. They fear that some Japanese companies might

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Japanese patent office: unlikely to recognize patents on *ex vivo* gene therapy.

be reluctant to invest the time and resources needed to develop gene therapy techniques, if the NIH patent leads foreign companies to dominate this area, and restricts access by Japanese companies to the United States, the world's single largest health-care market.

Japan is only now ramping up its gene therapy effort. Its first gene therapy trial was approved only recently, almost five years after the first trial began in the United States. Moreover, the vector to be used in the Japanese trial will be supplied by a company in the United States.

"If the award of this patent discourages Japanese companies who are now considering gene therapy research and development from continuing this research, it would be a real problem," says a senior official at the Ministry of Health and Welfare. "Japanese doctors dislike the patenting of medical therapies: It is not considered appropriate. There is a trend in the US to patent everything. There seems to be a fundamental difference in philosophy concerning these matters, which could lead to future trade friction," the official says.

Some researchers have gone so far as to ask the relevant Japanese scientific societies to issue a statement condemning the patent award. But Shegetaka Asano, General Secretary of the Japanese Society of Gene Therapy, argues against this. He believes it would not be good for the development of gene therapy in Japan and calls for the research community to take a more pragmatic approach in the hope of developing more of "an intimate collaboration" with the NIH.

Meanwhile, the research focus in Japan seems to be shifting from *ex vivo* to *in vivo* techniques. Many Japanese pharmaceutical companies see a greater potential for developing profitable clinical applications using *in vivo* techniques, which they hope will ultimately be used on an outpatient basis. These so-called second-generation, direct gene therapy approaches include the use of gene guns, direct injections into muscle, and the use of liposome formulations.

According to Masamoru Hasegawa, Managing Director of DNAVEC, a recently established gene therapy research and development company set up with government assistance by a consortium of seven large Japanese drug companies, the NIH patent has no bearing on Japanese research at the moment. DNAVEC is planning to conduct research in both *ex vivo* and *in vivo* gene therapy technologies.

RICHARD NATHAN

Takeda links up with SmithKline to tap into human genome database

Takeda Chemical Industries, Japan's largest pharmaceutical company, signed a letter of intent in late March with SmithKline Beecham, Britain's second largest drug company, to enter into a research collaboration to develop new drugs.

Under the agreement, Takeda will gain access to SmithKline's genomic technology, including the human sequence data that SmithKline has licensed from US-based Human Genome Sciences (HGS).

Drug company analysts speculate that Takeda has made this move because it fears that foreign companies are beginning to dominate in the area of gene patents, and in the hope that it will help consolidate its position in Japan and allow it to apply the genomic information to drug discovery.

However, a question mark still hangs over the ownership and intellectual property rights of genetic information. And there has been vigorous debate on whether this information should all be in the public domain. In September 1994, Merck, the largest drug company in the United States, responding to concerns that SmithKline could dominate in this area, announced plans to finance a 'public domain' sequencing project.

According to one industry analyst in Tokyo, Takeda is taking a gamble on this type of research. He points out that it will take a large number of researchers to make a go of this difficult and high-risk business. It is very difficult to create new drugs from genetic information alone. A clear understanding of a gene's function is also necessary.

Once the collaboration with SmithKline is finalized, Takeda, the world's 18th largest drug company by capitalization, reportedly will be shifting up to 50 of its best researchers to work on human genome analysis.

The gene business in Japan certainly seems to be at a turning point. Seven Japanese drugs companies — but not Takeda — have recently formed a collaborative, semiprivate gene therapy research and development venture (*Nature Medicine* **1**, 291; 1995). At least for the time being, Takeda is expected to remain independent of this group, opting instead to work closely with SmithKline.

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