that threaten to put at least a minor dent in UT's plans. The most conspicuous of these is the recent drop in oil prices.

This is having a two-pronged impact on the university's finances. It is slowing the growth of the permanent fund and playing havoc with state revenues, which in turn could mean smaller increases in appropriations for higher education.

Last year, university officials were predicting that the permanent fund would climb to more than $4 billion by the early 1990's, and that it would yield over $300 million a year in income—more than double the current available fund. If oil prices remain depressed for a few years, the fund will grow more slowly, but it is still expected to reach $3 billion by the end of the decade.

That level scarcely suggests that UT is entering a period of financial hardship. But the problem is that just as the growth rate of the permanent fund is tapering off, more claimants are clamoring for its resources. Under the state constitution, only certain units of the UT system can now use construction money generated by borrowing against the permanent fund, but a bill before the legislature would make the entire system eligible for a share in the pot. (The units that would be added are mostly those parts of the system that have been established in the past decade or so.) As a result, construction funds are likely to be stretched more thinly. The university has therefore proposed that the borrowing limit be raised from 20 to 30 percent of the value of the permanent fund. That would increase the total available for construction, but it would also mean that more of the income from the permanent fund would be tied up in paying off the debt.

A trend that may bring some relief from these difficulties is a slowdown in the growth of students entering higher education, which means that the demand for new classrooms, dormitories, and similar buildings will ease. In the past 4 years alone, the student population at UT Austin has expanded from 40,000 to 48,000. But, thanks partly to tighter admission requirements, last fall's enrollment leveled off.

Even if oil prices remain depressed and the resources derived from the permanent fund are spread more thinly, however, UT has clearly got itself into an enviable position. "We are part of the general economy, and I don't expect we can go entirely unscathed," says Flawn. But, unlike many other public universities that are having to cut back to cope with budget shocks, UT now has a substantial cushion.—**COLIN NORMAN**

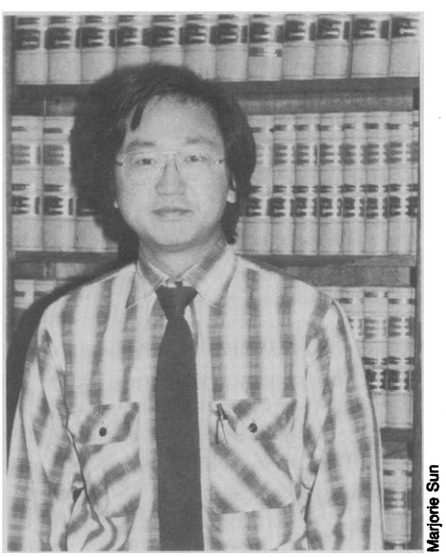
Scientists Settle Cell Line Dispute

But question of claiming ownership based on family ties to cell donor is sidestepped

San Diego—In July 1982, Ivor Royston, an oncologist at the University of California at San Diego, learned a bit of news, disclosed in passing at an office party, that he says "blew my mind." Royston was told that a visiting Japanese researcher had carried off part of a promising new cell line without permission. Hideaki Hagiwara had taken the cells back to Japan, hoping eventually to treat his mother, who was dying of cervical cancer. The cell line was a hybridoma, which is a fusion of two cells and a type of gene-splicing product of enormous scientific and commercial interest.

In the months to come, Royston, an associate professor, and Hagiwara, a young postdoctoral fellow, became embroiled in a debate over rightful ownership of the hybridoma, and proper credit for the research. The controversy was considerably complicated by another factor: the hybridoma was derived from cells taken from Hagiwara's mother. In an unusual argument, Hagiwara claimed ownership of the cells because of family ties. Last month the dispute was finally settled.

The cell line had a rare combination of properties that the researchers had not seen in other hybridomas. Researchers hope to use the monoclonal antibodies made by hybridomas as a possible cancer treatment. The hybridoma in dispute was a fusion of lymphocytes from Hagiwara's mother and human cells called UC 729-6, an established cell line developed at San Diego. In preliminary tests in Royston's lab, this hybridoma produced a monoclonal antibody which did not react with samples of normal cells, such as blood and fibroblasts. The test results were encouraging and an indication that the antibody might not cause side effects if administered to a cancer patient. Furthermore, the antibody did react with cancerous cells from the cervix, lung, colon, and prostate. According to Royston, no other human-human hybridoma has shown similar behavior.



Marjorie Sun

Hideaki Hagiwara

Carried the cell line to Japan

Hagiwara and Royston contested ownership of the cells, each claiming the more significant contribution to the project. Hagiwara, in addition to arguing a familial relationship, said it was he who proposed the idea of the fusion and that Royston's lab had simply carried out the technical task. Royston, however, maintained that his group actually created the hybridoma. Hagiwara "didn't realize the art and expertise involved," Royston says.

As details of the case unfolded, Royston became increasingly suspicious that the Japanese scientist had spirited away the cells to exploit them commercially. He learned, for example, that Hagiwara's father, a physician, is owner of the Hagiwara Institute of Health and president of Japanese Pharmaceutical Development Company, Inc., a health food concern. He discovered that Hagiwara had written a manuscript about the hybridoma that had not included Royston's staff as coauthors. Further-

more, he learned that Hagiwara had actually applied for a patent on the hybridoma in Japan.

Royston was concerned that the university might have lost its chance to patent the hybridoma. The other possible loser in the matter was Hybritech, a biotechnology company that funded part of the hybridoma project and would have claim to an exclusive license. Royston is a minor shareholder in the company.

Hagiwara maintained throughout the dispute that he was only trying to help his mother. A biochemist and graduate of Osaka University, Hagiwara came to San Diego in September 1981 to work as a fellow with Gordon Sato. Sato, a cell biologist, studies hybridomas made from mouse cells.

Two months later, Hagiwara learned that his mother was dying of cervical cancer and persuaded researchers in Royston's laboratory to develop a hybridoma using his mother's cells. Royston researches human hybridomas. According to Royston, there was a tacit understanding that if the monoclonal antibody passed rigorous testing—and the chances seemed slim—it might be used to treat his mother. Royston estimated that the testing might take a year or so.

Hagiwara hand-carried a preparation of his mother's lymphocytes from Japan to Royston's lab. There, Mark Glassy and Harold Handley achieved surprising success in January 1982 when they fused the two cell lines. Subsequent test results were encouraging.

At Hagiwara's request, Royston then gave him a split of the hybridoma culture to take back to Sato's lab to conduct his own experiments. By then, Hagiwara was frequently flying back and forth to Japan to visit his mother. On 2 July at an office party, Hagiwara himself said, in response to a question by Glassy, that he had taken some of the cells back to Japan. Glassy said, "I was shocked."

Asked if he requested permission to take the hybridoma to Japan, Hagiwara said in an interview that his immediate adviser, Gordon Sato, did not tell him that he needed authorization. But Glassy says that he told Hagiwara several times that Royston must authorize removal of the cells from the premises. Glassy and others were concerned that Hagiwara might prematurely take the cells to treat his mother.

And, indeed, that's what happened. Royston wanted to conduct more extensive testing on the antibody and also to obtain clearance from the university's institutional review board before considering treatment. But Hagiwara proceeded to administer the antibody to his mother without Royston's knowledge.

Hagiwara did exercise some precautions. In Japan, the cells were grown in mass culture at the Hagiwara Institute of Health and then further tested against other tissues. More purification was conducted. After checking with Japanese authorities, he says, he went so far as to inject the antibody into himself, his father, and three volunteers from the institute to check for adverse side effects. Hagiwara says there were none. His mother was then injected with the antibody. Royston says that the treatment may be the first recorded use of human-human hybridoma antibody in cancer therapy.

Marjorie Sun

Ivor Royston

Created a human-human hybridoma

It is not clear whether the cancer responded at all to the therapy. Hagiwara says that the doctors are still analyzing their data and declines to offer his own assessment. He will only say that the treatment helped his mother psychologically because it gave her hope.

As the controversy in San Diego mounted, Hagiwara resigned from the university. When asked if Hagiwara was asked to resign, Royston said, "No comment."

The turning point in the dispute came when Japanese newspapers picked up on American coverage of the matter. Some of the Japanese newspapers went further than U.S. reporters, stating that Hagiwara had stolen the cells. The allegation of theft embarrassed the Hagiwaras who sought a quick resolution. Within about a month, the parties reconciled their differences.

The agreement assigns the patent rights to the University of California and gives the Hagiwara Institute of Health exclusive license in Japan and other Asian countries. The institute will pay the university royalties if the hybridoma proves commercially valuable. In addition, Royston and Hagiwara agreed to exchange information generated from future research on the cell line. In fact, Royston's lab and Hagiwara, who is back in the United States, are currently preparing a manuscript together.

Both sides describe the agreement as "reasonable." Royston and university administrators have concluded that Hagiwara had only his mother's welfare at heart and was driven by a desperate attempt to save her life. She died last February despite treatment with the antibody made by the hybridoma.

All have agreed that the problem arose in part from a lack of understanding of each other complicated by language problems.

One matter that was sidestepped in the settlement is the question of ownership based on familial ties. Bertram Rowland, a patent attorney at Townsend and Townsend in San Francisco which represents the University of California, believes that the issue is not important. The critical consideration is to determine the inventors of the hybridoma, he says. A hybridoma, he points out, is a newly created biological entity. Therefore, ownership based on a being the donor or a relative, is irrelevant. The hybridoma in the Hagiwara case "no longer belonged to the mother because it's a fusion," Rowland says.

Royston says that to preclude the issue in the future a patient's informed consent form may have to be broadened. The statement currently gives a researcher permission to conduct research on a patient's tissue. Attorney Rowland suggests that it also include a statement that says cells "may be used for any purpose," and that compensation should not be awarded if the cell proves to be commercially lucrative.

Sato takes a different position. He believes that cell donors should automatically be given a share of any subsequent profit. Hagiwara's attorney, Harold Jackson of Jackson, Jones and Price in Tustin, California, asks, "Why should a scientist be the owner, if he has just fused it?" Ownership of a cell line "is an area of law that needs to be explored."

In any event, Hagiwara—whatever his motives were to take the cells—is setting aside the ownership issue. "This research is only the beginning," he says. "That's why I want to settle. Argumentation is worthless for the science."

—MARJORIE SUN