Research News

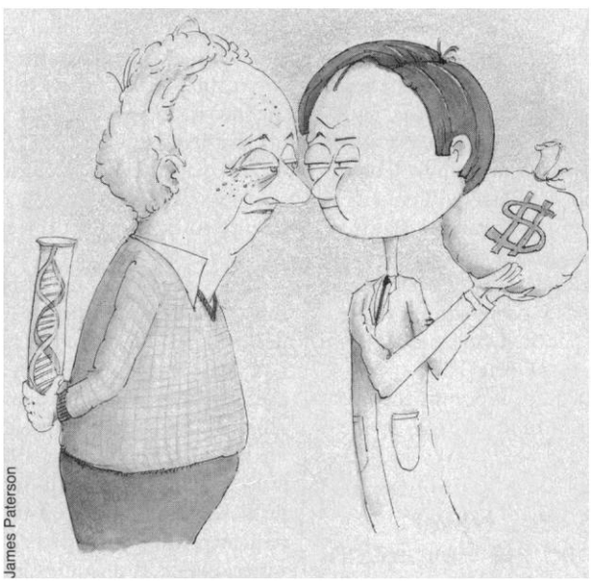
Watson versus Japan

James Watson is threatening to deny Japanese scientists access to DNA sequence databases unless Japan pays its "fair share" for the genome project

"I'M ALL FOR PEACE, but if there is going to be a war, I will fight it," declared James Watson, head of the genome project at the National Institutes of Health, at a recent meeting in San Diego.*

The war—so far more of a verbal tussle—is with Japan over that nation's contribution to the genome project. Watson has accused Japan of "freeloading." The Japanese, in turn, accuse him of "Japan-bashing."

The confrontation began several months ago when Watson wrote a letter to a Japanese scientist berating the Japanese for their parsimony and threatening—between the lines, at least—to deny Japan access to U.S. data unless it coughs up money for the genome project. The war went public on 19 October when Watson reiterated before Congress what he has been saying in private for some months: if other countries don't pay, they won't get to play.



James Paterson

To many in the biological community, the 61-year-old Nobel laureate has long been something of a wild man, and his colleagues tend to hold their collective breath whenever he veers from the script. With this latest incident, however, even those who share Watson's frustration with the Japanese think that he may have gone too far.

One friend calls his letter and subsequent comments "shocking" and "uncalled for." "Too much shooting from the hip," says another. The Japanese scientists privy to the affair are said to be deeply offended.

Watson, however, is unrepentant: "I've found you never get anywhere in the world by being a wimp," he said in an interview with *Science*.

The issue, Watson says, is whether the United States will pay billions of dollars to work out the complete DNA sequence of the human genome—all 3 billion base pairs—and then hand it over to the Japanese pharmaceutical industry. "It is against the American national interest to work out the human genome and pass it out free to the rest of the world," Watson declares.

*Human Genome I, sponsored by *Science*, 2 to 4 October.

Without question, the Japanese have gotten off to a slow start on their genome project, although it didn't always look that way. Indeed, in 1987 Akiyoshi Wada of the University of Tokyo announced that Japan was developing the capability to sequence 1 million bases a day—a phenomenal rate—for a mere 17 cents a base. The implication was that Japan was moving into the genome project in a big way.

It turns out, however, that Wada greatly oversold the capabilities of Japan's small sequencing technology project, which he headed at the time. Last year Wada's replacement, Yoji Ikawa, said that the goal had been scaled back to 100,000 bases a day.

Although there is still talk of a major Japanese effort and several new programs were recently launched, the Japanese initiative remains modest and fractured among four agencies. The Japanese are spending about $8 million, as compared with $90 million in the United States, for 1990 (*Science*, 27 October, p. 439).

What really gets Watson's goat is that Japan has not kicked in funds for HUGO, the international human genome organization that was conceived a year and a half ago at Cold Spring Harbor Laboratory, which Watson directs while running the genome project for NIH. To Watson, the only way to reduce the cost of this gargantuan project, estimated at $3 billion, is for various nations to divvy up the task and pool their resources. And Watson is counting on HUGO to ensure that these national efforts are coordinated and not duplicative. At this stage, however, there are serious doubts about whether HUGO is up to the task.

The solution, Watson thinks, is more money for HUGO—in particular, yen. From the start, the idea has been that the United States, Europe, and Pacific Rim nations would split the cost of running HUGO, estimated at $1.5 million a year. The Howard Hughes Medical Institute has been supporting HUGO in the United States, providing an office in Bethesda, among other things. The Imperial Cancer Research Fund in England recently kicked in, and an office will open sometime soon in England. Several governments and foundations are talking about contributions for next year. But "we haven't got a cent from Japan," snaps Watson, and plans for the Japanese office are on hold.

Thus, the letter, which Watson wrote to Kenichi Matsubara of Osaka University, head of the Ministry of Education's new Human Genome Program, in July. In the letter Watson canceled a scheduled trip to Japan, saying he would not visit until Japan agrees to support HUGO and generally gets its act together on its genome project. All this was couched in "Watsonian rhetoric," says Victor McKusick, a Johns Hopkins geneticist who is president of HUGO.

In the letter Watson spelled out exactly what he wants: $300,000 a year, if Japan wants to be considered a "great nation." Anything less, he warned, would imply a "halfhearted commitment" and could be the source of "continuing ill will and resentment." Moreover, said Watson, it would suggest that Japan is not serious about a major genome initiative.

"Japan should no longer expect to benefit from the generosity of other nations if it decides to remain outside the HUGO sphere," Watson wrote. The not at all subtle threat, which Watson had made explicitly at a meeting in Moscow a month earlier, was

to withhold sequence data by somehow denying Japan access to U.S. databases.

"It is a very bad letter," concedes Norton Zinder of Rockefeller University, a longtime friend of Watson and chairman of the genome advisory committee at NIH. "You should have seen the original draft," he moans. "Had he sent that, Japan would have withdrawn its ambassador. The trouble with Jim is he is often right but not very polite." Meanwhile, McKusick, who says he has no complaints with the Japanese, is in Japan on a fence-mending mission.

In private Matsubara, who has been pushing for a bilateral agreement on the genome project, has characterized Watson's letter as "Japan-bashing." To *Science*, however, Matsubara strikes a diplomatic tone, saying that "there are certainly some tensions between Watson and Japan over the genome efforts. However, I believe the problems are not really serious." But should Watson make good on his threat, says Matsubara, "we shall be extremely annoyed."

One of Matsubara's colleagues in the Human Genome Program, Nobuyoshi Shimizu of Keio University School of Medicine, likens Watson's comments to "blackmail." Shimizu does not argue with Watson's point that Japan should repay the generosity shown it since World War II, "but in what way and in what capacity is our decision."

Shimizu and Matsubara are also somewhat perplexed about whether Watson actually has the authority to make good on his threat. Nor are they clear about whether he is writing as the director of the NIH genome project, a member of HUGO, or a private scientist. Says Shimizu: "I am concerned, even if it is his private view, because he is very influential."

To Shimizu fell the thankless task of delivering Matsubara's response to Watson, which he did at the San Diego meeting in early October. The message, in brief, was that while Japan is in the throes of setting up its own project, "we do not have the time or money to contribute to any other country yet." Shimizu and Matsubara say that Japan fully intends to contribute its fair share to the worldwide genome project, but that it may take a few years. Shimizu asked Watson to be patient, explaining that the Japanese bureaucracy runs very slowly.

Watson, however, is clearly exasperated with talk of bureaucratic obstacles. "Just because the Japanese bureaucracy runs slowly, there is no reason for the U.S. to carry the burden," he told *Science*. "The Japanese must face up to the fact that they are a wealthy nation and act accordingly. When they have the money, we can talk."

Watson apparently has no qualms about retreating from the stance of scientific openness that he has always defended, though he admits it is not a popular position. "The genome project is an immense opportunity. . . . The thought that we might keep the data secret is terrible, but I don't see an alternative," he told *Science*. "If we have done it and paid for it, why give it up? We would have to have holes in our head. Sharing is sharing cost as well."

How, exactly, Watson would deny Japanese scientists access to U.S. databases is not clear, "but there are ways to make it difficult for them," sighs Zinder, who, along with everyone else *Science* spoke with, opposes the idea. Nor is Watson worried about offending his Japanese colleagues. "I believe the message should be unambiguous, otherwise you can waste a lot of time."

Meanwhile, Watson's colleagues are doing their best to distance themselves from his remarks. "Watson is speaking for himself," says George Cahill of Howard Hughes Medical Institute and treasurer of HUGO. "He does not speak for NIH or HUGO. He does not speak ex cathedra like the Pope."

Not everyone takes offense at Watson's saber-rattling, however. In fact, one Japanese biologist at the recent San Diego meeting said he loves it, noting that every time Watson says something outrageous, the Japanese government boosts its support for the genome project.

And that, after all, is what Watson wants.

■ LESLIE ROBERTS

How Do You Read from the Palimpsest of Life?

A controversial new theory says that organisms of the ancient RNA world had a complex metabolism and used DNA—but had almost no protein enzymes

ABOUT 2.5 BILLION YEARS AGO, give or take a billion, Earth was populated by a one-celled organism that was very much like the bacteria of today, and yet eerily different. It obtained its energy much as today's lifeforms do. It probably even encoded its genetic information the same way, using DNA. And yet it had none of the protein enzymes that catalyze chemical reactions in modern organisms; instead it did its catalytic work with complex RNA molecules. It was also the ancestor of all modern life. It was "the breakthrough organism."

Or—maybe it wasn't. Building biochemical models of early organisms is an active and fractious growth industry these days. And the model above, which was recently proposed by organic chemists Steven A. Benner and Andreas Tauer of the Swiss Federal Institute of Technology in Zurich, and molecular biologist Andrew D. Ellington of the Massachusetts General Hospital in Boston, is more controversial than most.

"In reading their paper I wasn't sure if they were listening to nature or telling nature what to do," declares molecular biologist Alan Weiner of Yale University, their chief critic and a man who has done quite a bit of theorizing about early life himself. If nothing else, he says, "I find the whole notion of a 'breakthrough' organism ridiculous. It's unbiological. Things happen much more slowly than that."

Nonetheless, other researchers defend the work of Benner and his colleagues as one of the most ambitious and provocative reconstructions of early life to date. "The Benner paper is as rigorous as can be," says Harvard University emeritus chemist Frank H. Westheimer, who was an adviser for Benner's 1979 Ph.D. thesis. "It would be extraordinary if they got everything right. But they will certainly stimulate a lot of work."

"It's an extreme point of view," agrees chemist Leslie Orgel of the Salk Institute in La Jolla, California. "But I'm not willing to say it's wrong, either."

Benner, Ellington, and Tauer start out conventionally enough. Like most other origin-of-life researchers these days, they accept the idea that the primeval Earth was an "RNA world"—that is, a world in which RNA sequences were both a medium for storing genetic information and molecular workhorses directing the cell's metabolism through catalysis. Indeed, Thomas Cech of the University of Colorado and Sidney Altman of Yale University were just awarded the 1989 Nobel Prize in Chemistry for their discovery that RNA *can* function as a catalyst (*Science*, 20 October, p. 325).

Where the group goes well out on a limb, however, is in their attempt to describe what the RNA world was like. Instead of accepting most researchers' tacit assumptions that RNA catalysts were primitive and ineffectual, their model depicts an RNA world that was rich, complex, and vital. "If you believe