gaining more than 21% in a day. But academic scientists who had also chased this gene and, unlike HGS, published scientific papers showing that HIV uses the receptor, were dumbfounded—especially because HGS did not know of the AIDS connection when it filed its patent.

The patent decision "takes my breath away," says Robert Gallo, director of the Institute of Human Virology at the University of Maryland, Baltimore. "As a society, we have to ask if it's fair" to give the main commercial prize to the company that simply sequences a gene rather than to those who do the hard work of figuring out its biological function, says Gallo. Several groups, including Gallo's, that played critical roles in identifying the suite of receptors that HIV uses to slip inside cells have also applied for patents, but their claims were filed after HGS's. (A patent expert at the National Institute of Allergy and Infectious Diseases notes that the Patent Office could still issue other, competing patents on CCR5, creating a nasty legal traffic jam.)

> **"As a society, we have to ask if it's fair" to give the main commercial prize to gene sequencers.**
>
> **—Robert Gallo**

"I'm flabbergasted," says virologist Christopher Broder. "I can't believe" the Patent Office made a decision to reward what he calls "armchair" biology research by HGS. Broder, now at the Uniformed Services University of the Health Sciences in Bethesda, Maryland, was a member of a National Institutes of Health team led by Edward Berger and Philip Murphy that in 1996 published a detailed analysis of how CCR5 works as a "coreceptor" for HIV on the surface of immune system cells (*Science*, 10 May 1996, p. 872, and 28 June 1996, p. 1955). Berger was traveling and couldn't be reached for comment, but Broder said that "it is rather upsetting to all of us to learn that this company is obtaining patents, despite the fact that we made the discovery first." Murphy says he, too, was "a little surprised" by the patent. HIV researchers John Moore of the Aaron Diamond AIDS Research Center in New York City and Robert Doms of the University of Pennsylvania, Philadelphia, were also dismayed to learn that HGS's sequencing effort seems to have given the company priority over those who first published studies on CCR5's function.

But HGS's chief executive, William Haseltine, a former HIV researcher himself, says his company didn't simply churn through sequencing data to obtain priority. He says the company's strategy from the outset was to use sequencing as an entry point to research, and then to move quickly from databases to "wet biology" and pharmaceutical development. HGS targeted the family of cell receptors that includes CCR5—the seven-transmembrane group—for special attention because they have been hugely successful pharmaceutical targets. Drugs aimed at these receptors, which include antiulcer and allergy remedies, account for $40 billion in sales annually, he says.

Haseltine recalls that CCR5—which has a different name tag in HGS's database—turned up in a batch of unknown gene sequences in an early sequencing scan of the human genome begun in 1993. He says the company's computer analysis tagged it as a probable seven-transmembrane receptor, and it was cloned in a cell line and expressed. "Very quickly, we discovered that it was a chemokine receptor ... and we used that information to write that description of the gene in a patent," Haseltine says. The patent, filed in June 1995, included "many" other genes. He says HGS has 13 patents on receptors in this family. "We also realized that chemokine receptors might be viral receptors," Haseltine explains, so the patent was written to cover generic medical uses of CCR5, such as for therapies to block or enhance the function of the receptor.

Haseltine confirms, however, that the connection between CCR5 and HIV was not known when the initial patent was filed. Indeed, HGS's patent doesn't mention AIDS or HIV. But HGS's press release on 16 February 2000 describes the patent as covering "what is believed to be the critical entry point for the AIDS virus." HGS has licensed the patent to its pharmaceutical partners for AIDS drug development, including a new deal with Praecis Pharmaceuticals Inc. of Cambridge, Massachusetts, to develop "peptide mimetic drugs," according to Haseltine. HGS itself will try to develop antibody-based therapies to block or treat HIV infection.

Haseltine says he understands why other scientists are disappointed and agrees that they deserve recognition for their work in elucidating the function of CCR5. HGS, he claims, is ready to share data and reagents with them. "We would not block anyone in the academic world from using this for research purposes." But if anyone wants to use the receptor to create a drug, HGS will enforce its claim. **–ELIOT MARSHALL**

ScienceScope

Congress began looking over President Clinton's $43 billion civilian science budget request last week, with hearings on various agencies. Two reports from the front lines:

NIH Envy Building upon the generally positive reaction to the record $675 million increase the White House has proposed for her agency in 2001, National Science Foundation (NSF) director Rita Colwell is already out for more.

Asked last week by a very supportive House Science Committee if there were any "unmet needs" in the foundation's proposed $4.6 billion portfolio, Colwell didn't miss a beat. "I'd like to bring the size of our grants at least to the level of the average [National Institutes of Health] grant," she said, which at $300,000-plus per year is now about four times larger. Bigger grants would make scientists more efficient, she explained, by reducing the time spent submitting applications and reviewing proposals. Funding this year's request, she added, would allow NSF's average grant size to jump from about $80,000 to $108,000.

Colwell said she hoped to achieve the goal in 4 years. The cost? "It would take another $4 billion," she said coolly.

Show and Tell Last year's murmured worries that the National Institutes of Health (NIH) may not be able to spend its ballooning budget effectively appear to be growing louder this year. Appearing before a House appropriations subcommittee last week, NIH acting director Ruth Kirschstein fielded a bevy of questions about how the agency can ensure that a proposed $1 billion increase will go to high-quality science.

Challenged by subcommittee chair Representative John Porter (R–IL) to develop "convincing evidence ... that this money is being spent wisely," Kirschstein said that the agency is struggling to develop measures—from grant statistics to quality-of-life measures—that demonstrate good stewardship. "We have ideas but haven't quite gotten there," she said.

Few observers, however, expect the doubts to undermine congressional support for another NIH increase this year.

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