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Misconduct investigations on trial

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New ear cocked for E.T.

HIV TESTING

French AIDS Research Pioneers To Testify in Trial of Ministers

PARIS—Nearly 2 decades ago, Pasteur Institute virologist Luc Montagnier and a small band of French physicians and scientists were among the first to raise the alarm about the newly emerging AIDS epidemic. They went on to isolate HIV, the virus that causes the disease. This week, Montagnier and other members of this pioneering group began reliving those bygone days, but they are not participating in a cozy reunion. They are appearing as witnesses in one of the most highly publicized court cases in modern French history: the trial of former Prime Minister Laurent Fabius and two former ministers, who are accused of "involuntary homicide" and "involuntary assault on the physical integrity of persons" for having allegedly delayed measures to protect the nation's blood supply and blood products from contamination with HIV. The trial began on 9 February and is expected to last several weeks; if convicted, the defendants face up to 3 years in prison and heavy fines.

Witnesses. Luc Montagnier and Willy Rozenbaum (*above, left to right*) are among several researchers who have been called to testify in trial of former Prime Minister Laurent Fabius (*below*).

Nearly a dozen members of the original AIDS team have been called as witnesses, along with other leading French scientists such as Nobel laureate Jean Dausset, geneticist Axel Kahn, and Philippe Lazar, former head of the biomedical agency INSERM. In all, several dozen scientists, physicians, administrators, and politicians are expected to testify before the Justice Court of the Republic, a special court composed of jurists and parliamentarians that was created for trials of former ministers. The testimony of AIDS researchers is intended to shed light on the key scientific issues in the case: What did the ministers know about the AIDS epidemic, and when did they know it? In particular, the court will probe whether French authorities delayed the use of a blood test made by the U.S. company Abbott Laboratories, based on work by Robert Gallo and his colleagues at the National Cancer Institute, to give the French company Diagnostics Pasteur time to market its own version, based on the Montagnier group's work.

"We have been called to put things in the context of the knowledge of the time," says immunologist Jean Claude Gluckman of the Pitié-Salpêtrière Hospital in Paris, who was a member of the original AIDS team. But although some of the researcher-witnesses may share credit for discovering HIV, they have sharply differing views about the critical questions in the trial, which may make for contradictory testimony.

The case concerns the actions of Fabius and his two co-defendants—former Social Affairs Minister Georgina Dufoix and former Secretary of State for Health Edmond Hervé—during the critical period between 1983, when HIV was first isolated, and 1985, when measures to test and protect the blood supply went into effect in France. All three ministers are accused of having held up approval of the Abbott test in France for several months in 1985. Dufoix and Hervé are also accused of delaying HIV-destroying heat treatment of blood products destined for hemophiliacs until the existing supply of untreated products was exhausted. Finally, Hervé is charged with ignoring advice from health experts in 1983 to begin screening blood donors to eliminate high-risk individuals, including prisoners and others at risk of blood-borne infections such as hepatitis B. In previous trials, several physicians have already been convicted of related charges, and more than 30 other defendants may face trial in the scandal, which has now been dragging on for nearly 12 years (*Science*, 16 June 1995, p. 1563).

A key issue is whether financial considerations—particularly a desire to prevent Abbott from getting the upper hand in the AIDS-test marketplace—were decisive in these delays, or whether the government had other reasons to move slowly. Yet just how helpful the testimony of French researchers will be to the court is an open question. "I am very afraid that we will create more confusion than enlightenment," says Willy Rozenbaum of the Rothschild Hospital in Paris, one of the first physicians to treat AIDS patients in France. For one, few of them participated in the ministerial-level meetings at which key decisions were made. For another, notes Montagnier, testing decisions at the time were clouded by uncertainty about how many HIV-infected patients would actually go on to develop AIDS. "In early 1985, the first epidemiological studies indicated that around 10% of HIV-infected patients would get AIDS within 5 years, but then later it became clear that most would [eventually] get sick." On the other hand, Montagnier says, the difficulty in getting adequate government support for AIDS research in France during those early days probably retarded the development of AIDS tests and other measures to prevent infection with HIV. "The support we got was very low, and that probably delayed the research."

Given what was known at the time, says Rozenbaum, "I think the decisions of the prime minister were sound from a technical point of view." He adds that the high number of false positives given by early versions of both the French and American tests argued against immediately using them for widespread testing. Instead, Rozenbaum says, much more emphasis should have been put

CREDITS: (CLOCKWISE FROM LEFT) FLORENCE DURAND/SIPA PRESS; LOUIS ALLARD/SAOLA/CAMMA; WILLARD/SIPA PRESS

on screening out high-risk donors.

A very different view is held by immunologist Jacques Leibowitch at the Raymond Poincaré Hospital near Paris, one of the founders of the original AIDS group. In late 1984, months before the Abbott test was even approved in the United States, Leibowitch, working with colleagues at the blood bank of the Cochin Hospital in Paris, tested 2000 blood donors with an early, relatively nonspecific antibody test he had developed. Ten donors, or 0.5%, tested positive. Leibowitch says these findings were immediately communicated to blood bank and health authorities but were not made public until he and his co-workers leaked them to the French press months later. "As soon as this test was available, for moral and ethical reasons it should have been used," says Leibowitch. But others, including Rozenbaum and Montagnier, are not so sure. "Some people were skeptical about these test results," says Montagnier, "because the laboratory technique used ... had not been validated at the time and its specificity was put into question."

Whether or not these differing points of view will help clarify the issues before the court, they are sure to add some fireworks to the proceedings. "Even if this testimony is at odds, it will shed light on the information available to the political leaders of the time," says Kahn, a geneticist at the Cochin Institute, which is associated with the Cochin Hospital. Although Kahn is not an AIDS researcher, he told *Science* he believes that he has been called to testify both because of his experience in biomedical research and also because of a decision he made during a harrowing personal experience in 1985: Admitted to Cochin Hospital for a sudden hemorrhage, he refused a blood transfusion.

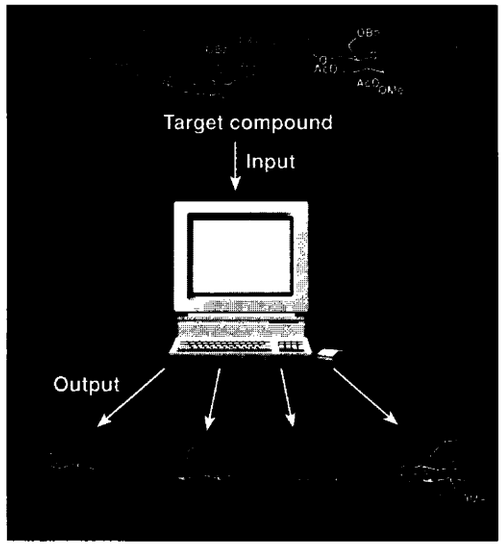
–MICHAEL BALTER

ORGANIC CHEMISTRY

Cooking Up Sugar Chains in a Hurry

Knitting together short chains of DNA or protein takes about as much work as cooking a microwave dinner. Just pop the molecular building blocks into an automated synthesizer, tell a computer what you want, and presto—out come tailor-made molecules, ready for testing as potential drugs and DNA probes, among other uses. But producing a third class of biomolecules—chains of sugar groups known as oligosaccharides—is more like cooking lobster thermidor without a recipe book. Now Chi-Huey Wong and his colleagues at The Scripps Research Institute in La Jolla, California, have come up with an easy-to-follow, one-pot recipe.

In a paper in last week's issue of the *Journal of the American Chemical Society*, Wong's team reports creating a set of sugar-based building blocks and a computer program for creating a range of oligosaccharides in one simple reaction. "It is very important work," says Samuel Danishefsky, an organic chemist and oligosaccharide expert at the Sloan-Kettering Institute for Cancer Research and Columbia University in New York City. By speeding the synthesis of these sugar chains, which are essential for everything from the ability of immune cells to recognize their targets to the spread of cancer around the body, the new scheme could help biologists pin down their precise roles. "We spend 95% of our time making the compounds," says Carolyn Bertozzi, a glycoprotein chemist at the University of California, Berkeley, who is working to parse out how oligosaccharides work inside cells. This new work "could help us turn that around" and spend 95% of the time on the biology, she says.



Master chef. When the structure of a desired oligosaccharide is fed into a computer program, it generates a list of standard building blocks to make the compound.

Creating biomolecules like peptides—short protein chains—is simple. Their amino acid building blocks are all linked with the same bond, making it straightforward to link several together like boxcars in a train. Oligosaccharides, by contrast, are more like a child's Lego bricks: They can snap together in many different arrangements and thus can form a myriad of three-dimensional shapes. The simple sugar glucose, for example, has four nearly identical points at which it can link with other sugars. And the bond that forms each link can itself take on two different shapes. The result is that glucose alone can react with a single partner in eight different ways—to say nothing of the configurations taken on by the partner. Try to string a few sugars together and "the problem becomes factorial," says Danishefsky.

The conventional approach to making a specific oligosaccharide is to bandage sugar molecules with "protecting" groups at all but one reaction site to block unwanted reactions. But that requires chemistry so complex, says Bertozzi, that Ph.D. students can spend a year just learning how to link two or three sugars together.

In the hope of speeding up the process, Wong and his colleagues picked up on a theme outlined over the last few years by Steven Ley and his colleagues at the University of Cambridge. The Cambridge team constructed a set of sugar-based building blocks, each preloaded with different protecting groups. They reacted the building blocks one at a time with a common sugar to find out how fast each reaction occurred. That allowed them to rank the reaction rates from fast to slow. They then selected different combinations of the building blocks and put them together in a single pot. The building blocks with the fastest reaction rate fused together first, while the next fastest reaction added a third component to the chain, and so on.

Wong's group expanded this strategy, adorning six different sugars with various combinations of protecting groups to alter the speed at which each sugar reacted. They ended up with a total of 50 different building blocks, which they ranked by reactivity. They then designed a computer program that allows users to type in the sequence of an oligosaccharide they want to make. The computer determines exactly which building blocks (with the protecting groups at the right places) must be added to the reaction stew so that the sequence of reactions, from fastest to slowest, produces the desired compound. The result is that making a two- to three-member

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