



Virus vanguards. Harald zur Hausen, Françoise Barré-Sinoussi, and Luc Montagnier will share this year's Nobel Prize in physiology or medicine.

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Nobel Prize Surprise

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In a snub to one of the world's most famous virologists, the Nobel Assembly at the Karolinska Institute in Stockholm, Sweden, announced today that it has awarded the 2008 Nobel Prize in physiology or medicine to Luc Montagnier and Françoise Barré-Sinoussi of the Pasteur Institute in Paris for their discovery of the virus that causes AIDS. The decision passes over Robert Gallo of the Institute of Human Virology at the University of Maryland School of Medicine in Baltimore, with whom Montagnier had a long-running battle over both credit for the AIDS virus's discovery and the patents related to the test used to detect the virus in blood.

Montagnier and Barré-Sinoussi together receive half of the \$1.4 million award; the other half goes to German virologist Harald zur Hausen for finding that the human papillomavirus (HPV) can cause cervical cancer. Although the HPV discovery ultimately led to two recently approved cancer vaccines now being widely introduced in developed countries, zur Hausen's prize has been overshadowed by the controversial choice of his fellow laureates.

The Nobel committee credits Montagnier and Barré-Sinoussi for first isolating the human immunodeficiency virus (HIV) from a French patient with swollen lymph nodes. The researchers also detected activity of an enzyme called reverse transcriptase, proof that the infectious agent belonged to a group called retroviruses, which insert their own DNA into the genome of the hosts.

But Montagnier's lab did not prove that their virus caused AIDS. That evidence first came 1 year later from Gallo and co-workers, who published four papers in *Science* that persuasively tied similar viruses they had found to the disease. Gallo says all three recipients of the prize deserved it, and he's happy to see that the Nobel Assembly at long last gave an award to the

HIV/AIDS field. But he acknowledged that he was "disappointed" to be left out. "Yes, I'm a little down about it, but not terribly," Gallo told *Science*. "The only thing I worry about is that it may give people the notion that I might have done something wrong."

"I'm very sorry for Robert Gallo," Montagnier told *Science* today from Abidjan, Côte d'Ivoire, where he is attending an HIV meeting. Montagnier says he was "surprised" as well: "It was important to prove that HIV was the cause of AIDS, and Gallo had a very important role in that."

Gallo, who was famously competitive with Montagnier and other labs during the race to find the cause of AIDS, also stressed that he's mellowed a lot. "Twenty-five years ago, I'd be stuttering and saying, 'What the hell is going on?' As long as everything is not taken away from my legacy, that's fundamentally what matters to me."

The decision not to include Gallo stirred mixed emotions among the HIV/AIDS research community, in particular because his lab played a critical role in developing the technology to grow HIV in culture dishes and also subsequently made fundamental discoveries about the genes of the virus and how it enters cells. "I am sad that Bob was left out," says Nobel laureate David Baltimore, who does HIV/AIDS research himself at the California Institute of Technology in Pasadena. "His work was critical to pinning down HIV as the cause of AIDS."

Hans Wigzell, an HIV/AIDS researcher at the Karolinska Institute in Sweden who chaired the Nobel committee for physiology or medicine from 1990 to 1992, says he's "always surprised" by the award decisions, but that panel members take seriously Alfred Nobel's original wishes. "They follow in a very strict sense the will of the donor in the sense that it should be given to a discovery," say Wigzell. "They never give it for lifetime achievement, and that, by many in the scientific society, is considered to be unfair."

The Gallo and Montagnier feud at its root is about apportioning credit, but it at first focused on the patents for the HIV blood test. In 1987, U.S. President Ronald Reagan and French Prime Minister Jacques Chirac calmed the legal waters by proclaiming the two researchers "co-discoverers" of the virus and agreeing to split the patent royalties between the two countries. Gallo and Montagnier accepted that compromise and buried the hatchet, even co-authoring a chronology of AIDS research that ran in *Nature* that year. The controversy stayed quiet until 1990, when the *Chicago Tribune* published a massive investigative story by John Crewdson, who questioned whether Gallo's lab had stolen the virus from Montagnier's group. That led to an investigation by the U.S. National Institutes of Health, Gallo's employer at the time, and the U.S. Congress became involved. But Gallo and his team ultimately were cleared of wrongdoing.

Gallo and Montagnier had a rapprochement in the late 1990s that culminated in each writing essays in *Science* in 2002 in which they concluded that both made important contributions to the discovery of the virus. "Over the past 20 years, the scientific and legal controversies between our team and Gallo's

group have faded," Montagnier wrote. The essays were seen by some as a way to prepare the ground for a shared, controversy-free Nobel award. Yet, "the protagonists don't get to write history themselves," says Pasteur researcher Simon Wain-Hobson.

At a press conference this morning, members of the Nobel Assembly made clear that what mattered most to their decision was the first discovery of the virus, not proving what caused AIDS or later agreements between the rival labs to share the credit and benefits. "When it comes to deciding who made Nobel Prize-worthy discoveries, I think we are the experts, not a set of lawyers," Hans Jörnvall, secretary of the Nobel Committee for Physiology or Medicine, said.

The other half of the Nobel honors goes zur Hausen's determined efforts to establish HPV's link to cervical cancer. When zur Hausen started working on the topic in the 1970s, at the German Cancer Research Centre in Heidelberg where he still has his lab, it was widely believed that cervical cancer could be caused by a sexually transmissible virus, says HPV researcher Joakim Dillner of the University of Lund in Sweden--but the agent was a matter of great debate. The herpesvirus was among the key suspects, but zur Hausen bet on HPV, which was known to cause warts. "Many people thought he was out of his mind," says Philip Davies, director-general of the European Cervical Cancer Association.

In 1983, zur Hausen was able to demonstrate the presence of HPV-16 and -18--two of many different HPV types--in cervical cancer biopsies. The two viruses were subsequently found in about 70% of cervical cancer biopsies throughout the world. "He showed the importance of innovative thinking in science," says Dillner--"that, and persistence." HPV has since been implicated in cancer of the vulva, anus, penis, and mouth. Zur Hausen says he felt vindicated--and was "completely surprised"--when he heard the news this morning shortly before the press conference in Stockholm began.