

The Nobel Prize in Physiology or Medicine 2008

“for his discovery of human papilloma viruses causing cervical cancer”

“for their discovery of human immunodeficiency virus”



DEUTSCHES KREBSFORSCHUNGSZENTRUM (DKFZ)

Harald zur Hausen

1/2 of the prize

Born: 1936

Birthplace: Germany

Nationality: German citizen

Current position:

Professor Emeritus and former Chairman and Scientific Director, German Cancer Research Centre, Heidelberg, Germany



SAKUTIN/SCANPIX

Françoise Barré-Sinoussi

1/4 of the prize

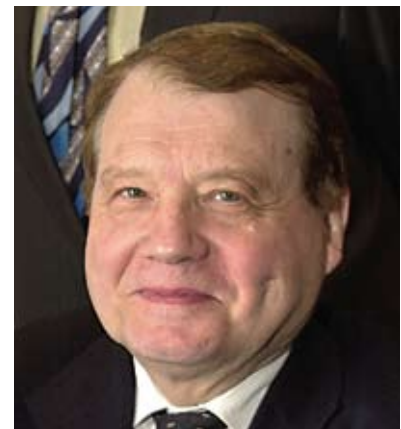
Born: 1947

Birthplace: France

Nationality: French citizen

Current position:

Professor and Director, Regulation of Retroviral Infections Unit, Virology Department, Institut Pasteur, Paris, France



MAGUNIA/SCANPIX

Luc Montagnier

1/4 of the prize

Born: 1932

Birthplace: France

Nationality: French citizen

Current position:

Professor Emeritus and Director, World Foundation for AIDS Research and Prevention, Paris, France

Speed read: Finding the culprit

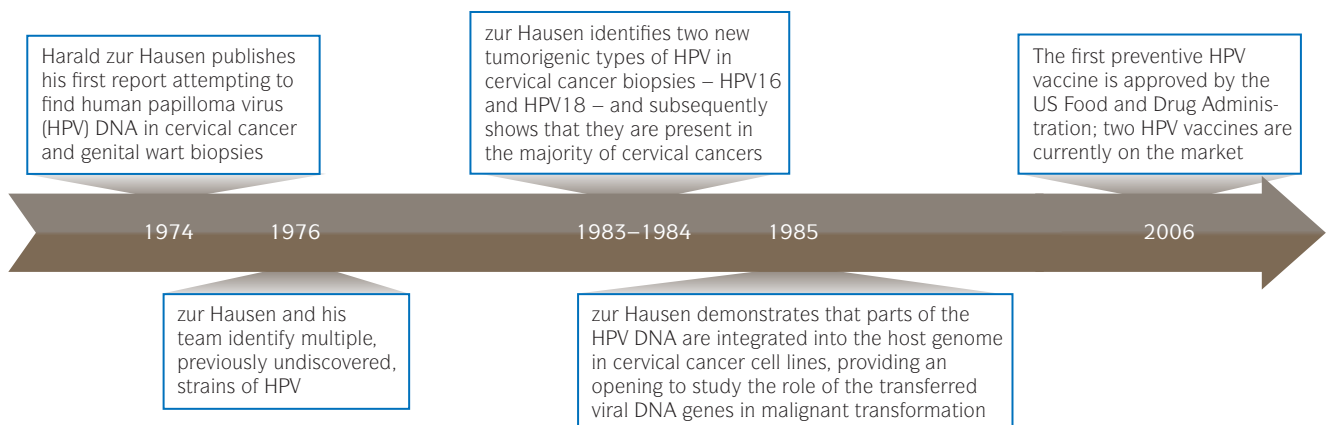


identification of the virus associated with AIDS, occurred within just a few months amid a flurry of global research activity directed towards finding the cause of the then-new epidemic.

Harald zur Hausen’s suggestion that human papilloma virus (HPV) infection might lie behind cervical cancer flew in the face of general opinion in the early 1970s, which held that another commonly present virus, herpes simplex virus, might be the cause. Realising that there were a multitude of different HPV subtypes, and hypothesising that unknown subtypes might cause the cancer, zur Hausen’s group began a painstaking search for such novel viruses. By the early 1980s they found novel viruses in genital warts. Their subsequent identification of two novel HPV subtypes in cervical cancers formed the essential piece of evidence linking HPV infection to the onset of the disease.

Looking back over the two discoveries rewarded with the 2008 Nobel Prize in Physiology or Medicine reveals two different timelines for discovery research. One, Harald zur Hausen’s realisation that subtypes of a virus that produces harmless warts can also lead to cervical cancer, took a decade of work to prove, initially against a backdrop of considerable scepticism. The other, Françoise Barré-Sinoussi and Luc Montagnier’s

discovery of the virus that later came to be known as human immunodeficiency virus (HIV) occurred



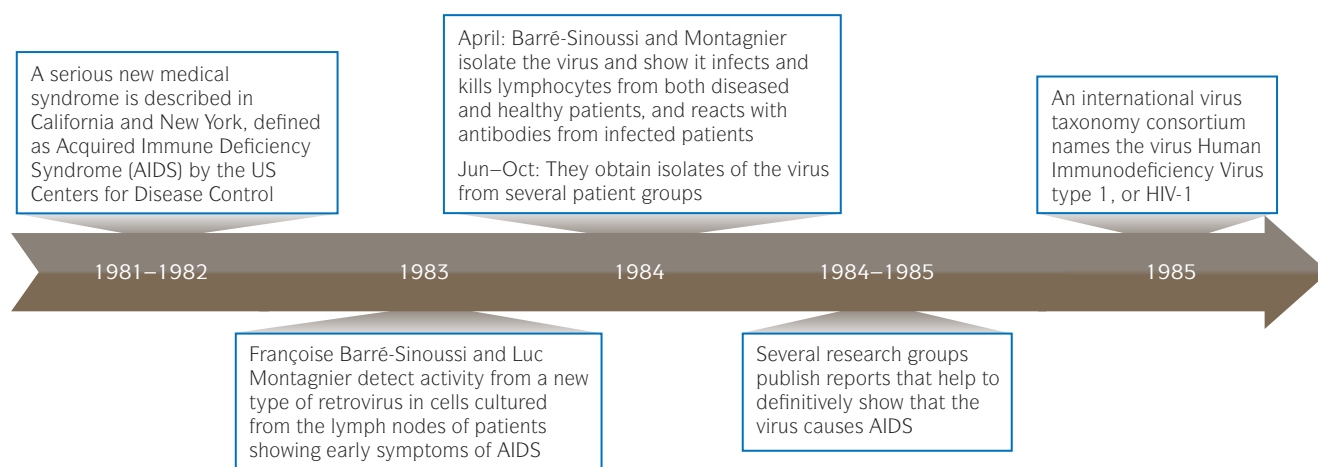
Timeline: Milestones for the 2008 Nobel Laureate in Physiology or Medicine, Harald zur Hausen.

just two years after the first reports of cases of what we now know as AIDS. An infective agent was suspected by many to cause the disease, and Barré-Sinoussi and Montagnier decided to test whether it might be a so-called retrovirus. Retroviruses are relatively uncommon among the viruses that infect humans and rely on the host's cellular machinery to replicate their RNA. The gamble proved correct; their studies revealed retroviral activity in cells taken from a patient's lymph nodes, and demonstrated that viral particles from these cells could infect and kill white blood cells. Within the year, Barré-Sinoussi and Montagnier had isolated HIV from several patient groups. Soon afterwards several research groups provided convincing evidence that showed HIV to be the cause of AIDS.

Identifying the viral culprits behind two human diseases that impact greatly on global health provided crucial insights into the workings of each virus, which, in turn, led to the development of much-needed treatments. zur Hausen's discoveries enabled the development of vaccines that provide



protection from the two HPV subtypes found in the majority of cervical cancer cases. Barré-Sinoussi and Montagnier's discoveries led to a greater understanding of HIV and the way it interacts with humans, allowing the development of diagnostic tools and a range of antiviral drugs aimed at controlling HIV, and with it providing hope that the disease could eventually become treatable.



Timeline: Milestones for the 2008 Nobel Laureates in Physiology or Medicine, Françoise Barré-Sinoussi and Luc Montagnier.

In his own words: Harald zur Hausen

"I'm of course totally surprised. And it's of course a great pleasure for me." Sitting in his office at the German Cancer Research Center, the news that Harald zur Hausen had received the 2008 Nobel Prize in Physiology or Medicine had yet to fully sink in. Perhaps surprise is an apt response; for years, few considered zur Hausen's proposal, that cervical cancer was caused by the same virus that caused skin warts, worthy of serious discussion, let alone a Nobel Prize.

When zur Hausen first suggested publicly that human papilloma virus, or HPV, caused cervical cancer at a meeting in Key Biscayne, Florida, in 1974, it flew in the face of the prevailing view that the culprit was herpes simplex virus. "It was not very welcome," recalls zur Hausen. "My statements were not well received, and I felt as a lonely voice in that meeting."

When asked what gave him the dedication to persevere for years and eventually prove the link between HPV and cervical cancer, zur Hausen responds that it was the combination of a personal conviction that there must be an infectious agent

involved in this cancer, together with the fact that so many questions remained unanswered about papilloma viruses. "I was not from the beginning mainly interested in papilloma virus, I was mainly interested in infectious agents in human cancer. Papilloma viruses came up as the most likely candidate from my viewpoint."

The key breakthrough in finding that two subtypes of human papilloma virus, called HPV16 and 18, are found in most cervical cancer cases wasn't automatically followed by the successful development of vaccines, mainly because companies were unconvinced that this was a worthwhile investment.

As zur Hausen recalls, one German company showed some interest, but it pulled the plug on the project after carrying out some damning market analysis.

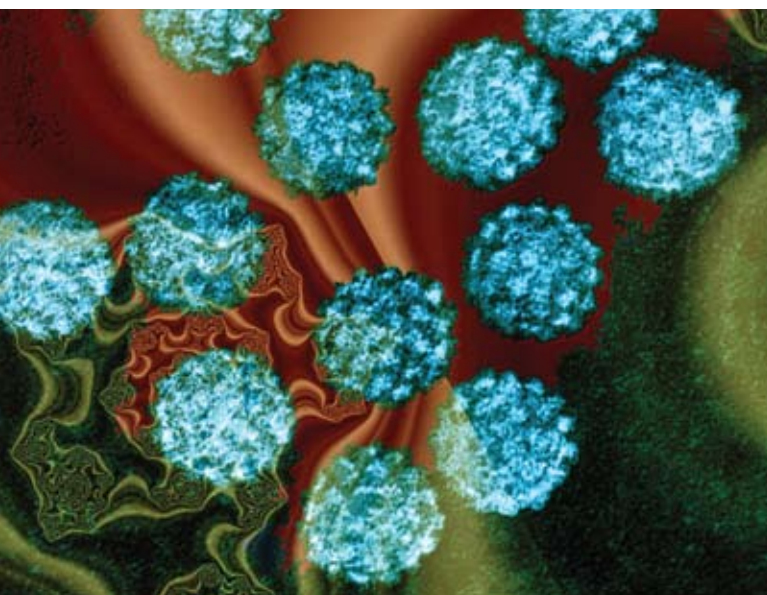
"According to this market analysis there would be no market for such a vaccine. And then they stopped the funding."

Now the opposite appears to be the case; results from trials on cervical cancer vaccines within the last decade have been enormously promising. zur Hausen sees this as clear evidence that vaccination programmes should be widened; however, he cautions that "The major disadvantage at this stage is that it is too expensive for those parts of the world which most badly need the vaccine; namely, the developing world."

zur Hausen believes that scientists will discover more links between viruses and cancer, and he is keen to promote greater interest in this line of research. "I hope, indeed, that this Nobel Prize will of course create more awareness of the role of infectious agents in human cancer".

Having spent decades in pursuit of his goal, it is perhaps appropriate that he hadn't rushed into making any plans for celebrating his Nobel Prize. "It was so surprising I really have to sleep about it for one night or so before I make any decisions."

"My statements were not well received, and I felt as a lonely voice"



Coloured transmission electron micrograph of human papilloma viruses (HPV).

DR LINDA STANNARD, UCT/SCIENCE PHOTO LIBRARY

This article is based on a telephone interview with Harald zur Hausen following the announcement of the 2008 Nobel Prize in Physiology or Medicine. To listen to the interview in full, visit http://nobelprize.org/nobel_prizes/medicine/laureates/2008/hausen-interview.html

In her own words: Françoise Barré-Sinoussi

Visiting the Pasteur Institute in Cambodia, Françoise Barré-Sinoussi says she was unaware that she had been awarded the Nobel Prize in Physiology or Medicine until a French radio journalist called her for an interview. “I didn’t know about the news. It was a big surprise.”

Barré-Sinoussi feels that Cambodia is an appropriate place to receive the happy news. “I’ve been working with developing countries since the mid-1980s and it’s really working with those countries that gives me another view, or another way, of orienting my research after the discovery of the HIV virus. It’s important to really know what’s going on in those countries strongly affected by these kinds of disease.”

“We said, okay, look, we have all the reagents, we have the technique, and so let’s try”

Recalling the discovery of the virus that later came to be known as human immunodeficiency virus, or HIV, Barré-Sinoussi remembers several waves of excitement as evidence slowly accumulated that she and her research colleagues had discovered a novel virus. “First it was the isolation of the virus from a patient that was with symptoms associated with AIDS. The second excitement was when we realised that it’s not a known virus. Then we had electron microscopy pictures showing that the morphology was different, and so on.” So, it was, as Barré-Sinoussi describes, a “progressive excitement”.

Looking for a retrovirus in the first place seems an inspired choice with the benefit of hindsight, though Barré-Sinoussi admits this was initially “because most of the other types of virus families were already being explored”. There were also “several lines of arguments” telling Barré-Sinoussi to look at retroviruses. “Since we were working on mammalian retroviruses at Pasteur at that time, we said, okay, look, we have all the reagents, we have the technique, and so let’s try.”



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Françoise Barré-Sinoussi says the discovery of HIV involved several waves of exciting findings.

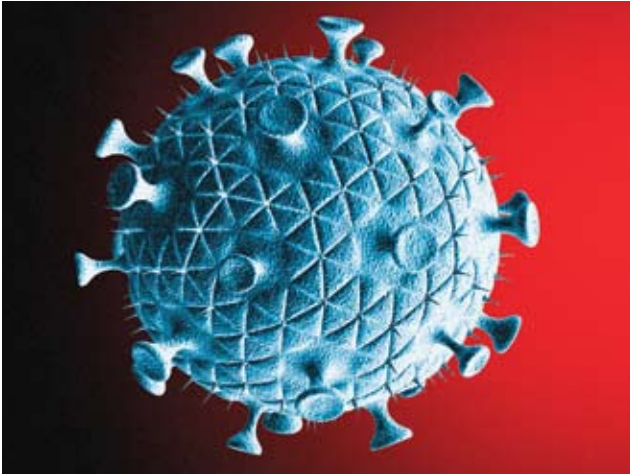
The educated guess paid off, and when asked what message she hopes her Nobel Prize will deliver, Barré-Sinoussi hopes that it highlights the fact that the success in discovering HIV is really the success of a global team of scientists, each bringing their different expertise to the task. “It’s also important, especially when working on infectious disease, to have a world network of clinicians, virologists and microbiologists, working in the hospitals and basic sciences. This was really essential for me in the discovery of the AIDS virus. And I think it’s essential also for tomorrow for discovering new, emerging, or re-emerging agents responsible for infectious disease.”

“I’ve been working with developing countries since the mid-1980s. It’s important to really know what’s going on in those countries strongly affected by these kinds of disease”



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In his own words: **Luc Montagnier**



Luc Montagnier and Françoise Barré-Sinoussi discovered HIV over 25 years ago.

On the day he heard that he had received the 2008 Nobel Prize in Physiology or Medicine, Luc Montagnier was attending an AIDS conference chaired by the President of the Republic of Ivory Coast, an indication that the battle against the disease is far from resolved. “Even after 20 years we are still fighting this virus very strongly, and the AIDS epidemic is still spreading in Africa,” says Montagnier, “so the fight is not finished.”

Montagnier thinks that tackling HIV, the virus that he and Françoise Barré-Sinoussi discovered in the early 1980s, requires urgent research into novel forms of treatment. “I know that in Africa it’s not possible to give a treatment for life. So the idea is to buy a treatment which, like for tuberculosis, could be given for a short period of time – 6 to 9 months – and then stopped.”

Such drug regimens could be supplanted with vaccines to eradicate the virus infection. Montagnier is developing one such treatment, not a preventive vaccine but a therapeutic vaccine, aimed at complementing the antiretroviral therapy given to many patients, so that their immune systems can defend themselves. “Nature has shown us a few percent of people which are in this stage. They are infected, they are not sick. So the idea

MEHAU KULYKSCIENCE PHOTO LIBRARY

“Even after 20 years we are still fighting this virus very strongly, and the AIDS epidemic is still spreading in Africa”

is to make most of these people, infected people, never sick, for life.”

Looking back on the moment that he and his colleagues first saw evidence of active HIV in cells taken from a patient’s lymph nodes, and that the virus from these cells could infect and kill white blood cells, Montagnier says he initially had little idea of the scale of the epidemic that he would be confronted with decades later. “But, when I realised that the virus could be the cause of AIDS and was present not only in gay men in France and the United States, and haemophiliacs, but also in African nations, I realised it could be big.”

In fact, Montagnier reveals that at the time of his discovery of HIV he was actually working on a possible viral cause of breast cancer, which he says makes sharing the Nobel Prize with Harald zur Hausen for his discovery of the viruses that cause cervical cancer a happy coincidence. “I’m still interested in cancer viruses so I appreciate that the Nobel Committee also has awarded the Prize to Harald zur Hausen who has worked for a long time on this.”

Luc Montagnier says the battle against AIDS in Africa is far from resolved.



This article is based on a telephone interview with Luc Montagnier following the announcement of the 2008 Nobel Prize in Physiology or Medicine. To listen to the interview in full, visit http://nobelprize.org/nobel_prizes/medicine/laureates/2008/montagnier-interview.html