

Scientist wins Nobel 3 days after cancer death (Update 2)

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In this April 24, 2009 photo, Dr. Ralph Steinman of Rockefeller University speaks during a news conference in Albany, N.Y., Friday, April 24, 2009. The Nobel committee says American Bruce Beutler and Luxembourg-born scientist Jules Hoffmann have shared the 2011 Nobel Prize in medicine with Canadianborn Ralph Steinman on Monday, Oct. 3, 2011. Beutler and Hoffman were cited "for their discoveries concerning the activation of innate immunity." Steinman was honored for "his discovery of the dendritic cell and its role in adaptive immunity." (AP Photo/Mike Groll)

Rockefeller University in New York says Ralph Steinman, <u>co-winner of</u> <u>this year's Nobel Prize in medicine</u>, has died.

Ralph Steinman, a pioneer in understanding how the cells of the body fight disease, tried to help his own immune system thwart his pancreatic



cancer.

Steinman survived until Friday. Three days later, he was awarded the Nobel Prize.

The Nobel committee, unaware of his death, announced the award Monday in Stockholm. Steinman's employer, Rockefeller University in New York, learned he had died only after the Nobel announcement.

Steinman's wife, Claudia, said the family had planned to disclose his death Monday - only to discover an email to his cellphone from the Nobel committee.

Friends and colleagues were stunned by the news of his death.

"For the last five years, I've gotten up in the morning of the Nobel Prize announcement and rushed to the computer to see his name," said Olivera J. Finn of the University of Pittsburgh.

"And this morning I saw it, and I just totally shrieked with joy," she said. Then she heard the bad news from a friend in Singapore.

"I have been this whole morning ... out of breath like somebody punched me in the stomach," Finn said.

Experts disagree whether Steinman's research helped him live for 4 1/2 years after he was diagnosed. A colleague in his lab thinks it did: The odds of making it even a year with his type of cancer are less than 5 percent.

Nobel officials said they believed it was the first time that a laureate had died before the announcement without the committee's knowledge.



"It is incredibly sad news," said Nobel Foundation chairman Lars Heikensten. "We can only regret that he didn't have the chance to receive the news he had won the Nobel Prize. Our thoughts are now with his family."

Since 1974, the Nobel statutes don't allow posthumous awards unless a laureate dies after the announcement but before the Dec. 10 award ceremony. That happened in 1996 when economics winner William Vickrey died a few days after the announcement.

However, the committee said Monday that Steinman's prize would stand and that his survivors would receive his share of the \$1.5 million prize money.

Steinman, 68, was awarded the prize along with American Bruce Beutler and French scientist Jules Hoffmann. They were honored for discoveries about the body's disease-fighting immune system.

Steinman discovered so-called dendritic cells in 1973. These cells regulate the activity of other cells - Steinman called them the conductor of the immune system.

"When he got sick, he realized he needed to call upon these cells to induce a strong enough immune response to fight his tumor, and that is what he did," said Dr. Sarah Schlesinger, clinical director for his lab.

Steinman tried eight to 10 experimental therapies approved by the federal government, focusing in various ways on revving up his immune system to fight his cancer, she said.

Colleagues came forward with the best approaches they had for other kinds of cancer, and Steinman analyzed what seemed the most promising for him, said Schlesinger, who helped him tailor the treatments for his



disease.

In one approach, for example, samples of Steinman's own dendritic cells were loaded with protein markers from his tumor, and then reinjected into his body. The idea is that this would "teach his immune system how to respond to that tumor," said Rockefeller colleague Dr. Michel Nussenzweig.

Although he also underwent chemotherapy, "he didn't really want to take it because he wanted to be cured," Nussenzweig said. "And he felt the immune system would be the best way to effect a cure, as opposed to just living with the disease."

Dozens of scientists around the world pitched in on the effort, Nussenzweig said. "Ralph was a special person, and they were all eager to do anything to try to cure him."

The experimental therapy continued until just recently, he said, but "there's no way of knowing whether it worked or not."

Steinman was the only patient, with no control group - other patients with the same cancer for comparison, a scientific must for convincing evidence. "It's not the kind of experiment Ralph would have liked to have done."

Rockefeller University said "his life was extended" using the therapy of his own design. Schlesinger believes that, pointing to the poor survival odds for his tumor and his good quality of life during his treatment. Noting he also got chemotherapy, she said, "I think it all worked together."

But Dr. Alan Venook, a pancreatic cancer specialist at the University of California, San Francisco, cautioned against drawing conclusions about



the impact of the treatments.

He said surviving four years with pancreatic cancer "is a long time," but not out of the question, depending on the type and how advanced it was when it was found.

"It's a disservice to the field for anyone to say that his immune therapy prolonged his life," Venook added.

"The phones will be ringing off the hook" with desperate patients who mistakenly believe that these experimental treatments have been proved safe or effective when in fact they have not, he said.

Finn said Steinman used several experimental therapies based on the immune system "because he believed in that as a solution to the problem of cancer." She said she believed the approach prolonged his life.

Nussenzweig said Steinman was working on his laboratory research until just a week ago.

He was open and honest about his cancer and "talked about it with a lot of people," Nussenzweig said.

"He was incredibly heroic in how he handled his disease," Finn said. "It was something important to fight. He continued his science, his publications, his experiments. He appeared at all the meetings. He received multiple prizes. He traveled.

"He wasn't delusional in any way, but he was not going to let the disease change his life. Science was his life, and he stayed with it until the end."

Hoffmann, 70, headed a research laboratory in Strasbourg, France, between 1974 and 2009 and served as president of the French National



Academy of Sciences between 2007-2008.

Beutler, 53, holds dual appointments at University of Texas Southwestern Medical Center in Dallas and as professor of genetics and immunology at the Scripps Research Institute in San Diego. He will become a full-time faculty member at UT Southwestern on Dec. 1.

Beutler and Hoffmann were cited for their discoveries in the 1990s of receptor proteins that can recognize bacteria and other microorganisms as they enter the body, and activate the first line of defense in the immune system, known as innate immunity.

The work of the three men has enabled the development of improved vaccines against infectious diseases, and in the long term could yield better treatments of cancer, rheumatoid arthritis, Type 1 diabetes, multiple sclerosis, and chronic inflammatory diseases, prize committee members said.

The work could also help efforts to make the immune system fight cancer, the committee said. A new treatment, Provenge, uses this concept to attack advanced prostate cancer.

Hoffmann said, "I am very touched. I'm thinking of all the people who worked with me, who gave everything. I wasn't sure this domain merited a Nobel."

Beutler said he woke up in the middle of the night, glanced at his cellphone and realized he had a new email message.

"And, I squinted at it and I saw that the title line was 'Nobel Prize,' so I thought I should give close attention to that," Beutler said in an interview posted on the Nobel website.



When he opened it, he saw that it was from Nobel committee member Goran Hansson, "and it said that I had won the Nobel Prize, and so I was thrilled."

The medicine award kicked off a week of Nobel Prize announcements, with the physics prize on Tuesday, chemistry on Wednesday, literature on Thursday and the Nobel Peace Prize on Friday. The winners of the economics award will be announced Oct. 10.

The coveted prizes were established by wealthy Swedish industrialist Alfred Nobel - the inventor of dynamite - except for the economics award, which was created by Sweden's central bank in 1968 in Nobel's memory. The prizes are always handed out on Dec. 10, the anniversary of Nobel's death in 1896.

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