Finding the cure

Harald zur Hausen shared a Nobel Prize for discovering the human papilloma virus, or HPV. His findings led to the development of vaccines against the two HPV strains that cause 70 percent of cervical cancers

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When German virologist Harald zur Hausen was declared co-winner of the 2008 Nobel Prize for Physiology or Medicine, he assumed his life would remain the same.

"At the time I was saying to people, no, it's not going to," he told the *Taipei Times* an hour before giving a lecture on cancer prevention to a packed auditorium of medical professionals and students.

"But I was suddenly flooded with e-mails, congratulations, interview wishes, invitations. So clearly that was an error," he said.

It was perhaps one of the few errors zur Hausen, 73, has made in a long and distinguished career as a physician and scientist.

Zur Hausen received the Nobel Prize for discovering the human papilloma virus (HPV) and the role it plays in the cause of cervical cancer. The importance of his breakthrough can be measured by the fact that he shared the prize with French virologists Luc Montagnier and Francoise Barre-Sinoussi, the two researchers who discovered the human immunodeficiency virus (HIV), which causes AIDS.

Zur Hausen's research findings led to the development of vaccines for two types of HPV — HPV 18 and HPV 16 — that cause 70 percent of all cervical cancers. Infection from HPV causes more than five percent of the world's cancers, and cervical cancer is the third most common cancer among women in Taiwan. Today, HPV is known to lead to vulval, vaginal and anal cancer in women, and cancer of the anus and penis in men.

In an interview with the *Taipei Times*, Zur Hausen touched on the science surrounding mad cow disease, the significance of sharing the Nobel with Montagnier and Barre-Sinoussi and the necessity of inoculating boys as well as girls against HPV.

Harald zur Hausen discovered the human papilloma virus, which causes cervical and other cancers. PHOTO COURTESY OF HARALD ZUR HAUSEN

Taipei Times: How did you feel when you won the 2008 Nobel?

Harald zur Hausen: I felt happy. I was pleased.

TT: You shared the prize with the Luc Montagnier and Francoise Barre-Sinoussi for their discovery of HIV. In your opinion, what is the significance of this?

HH: Let us look at HIV first. HIV is clearly a very important infection, which turns out to have enormous epidemic importance globally at the moment, so I think the discovery of the virus was an intensive hunting for quite a number of laboratories. And they were the first ones to do it. That's why they received it.

HPV is somewhat different because HPV was not really so much suspected to be a cancer-causing agent and for us it was a longstanding program which eventually turned out to be successful — particularly in 1983 and 1984 when we published the [HPV types] 16 and 18. But it was not, let us say, something that came quickly. It was really an elaborate period of time when we worked very hard to follow this type of idea with some disappointments in between.

TT: You began your career in the 1950s when the study of infectious diseases weren't a big area of study. How did your interests begin?

HH: As a schoolboy I had already firmly decided to become a scientist. This continued when I studied medicine and during the medical training I became aware of the fact that bacteria sometimes becomes infected by viruses, picks up some genetic material and modifies those properties. For instance, diphtheria bacteria gets its toxin by taking up a viral infection and that brought me to the idea that human cancer might be due to a similar phenomena — the uptake of genetic material from infecting agents and modifying the respective cells.

I have proposed this type of idea throughout my career: trying to link infectious agents to human cancer.

TT: It seems that during the 1970s and 1980s it wasn't a common idea.

HH: Let's put it this way: It wasn't a common idea that infections might be linked to human cancer. But it has been followed up since the turn of the last century and a couple of studies have been conducted that weren't successful over a long period of time.

TT: There seems to have been reluctance by the scientific community to accept your findings linking a virus with cervical cancers.

HH: There was a reluctance, indeed, but this was mainly due to a period of frustration over several decades. In spite of many attempts to find agents in human cancers there was no clear-cut evidence up to that time. But one thing that was not understood during this period of time was the long latency period, which turned out later to be a factor between virus infection and cancer development.

TT: On another level, vaccines for HIV and HPV are relatively expensive. In the past you've called for less expensive and easier ways to vaccinate young people.

HH: Well unfortunately, vaccines for HIV are not yet available. I mean there is a report of a partially successful vaccination, but it needs further confirmation.

But the vaccine for HPV, yes, you are quite right, they are too expensive in my opinion and there is really a need to reduce the prices drastically in order to make them affordable for those countries which at present are unable to buy them. I know, however, that both of the companies [that produce the vaccines] are reducing the prices in some of the parts of the developing world. But it's still too expensive. And so probably due to the fact that some competition is coming up, I presume there will be a drastic reduction.

TT: So competition is the thing that will bring down the prices.

HH: I guess so. Of course companies are interested in having a high income — they have high production costs, the clinical trials are very expensive. But it's not possible for a large part of the world to [pay] these prices.

(According to the Centers for Disease Control and Prevention, 50 percent of sexually active men and women in the US contract HPV at some point in their lives, and some 12,000 women are diagnosed with cervical cancer each year. Worldwide there are close to half a million cases, and more than 300,000 deaths. Eighty-five percent of deaths from cervical cancer occur in the developing world.)

TT: Although HPV is a virus that predominately leads to cancer in females, you've also suggested that males should also be vaccinated.

Harald zur Hausen in his laboratory. PHOTO COURTESY OF HARALD ZUR HAUSEN

> **"[T]here is really a need to reduce the prices [of HPV vaccines] drastically in order to make them affordable for those countries which at present are unable to buy them."**
>
> — Harald zur Hausen, Nobel Prize-winning virologist

HH: Very strongly. I feel that boys should be vaccinated. First of all it's a question of gender solidarity. It's also that ortho-cancers, which lead from this type of infection, occur more frequently in males than females, like cancer of the oropharynx. It occurs at least as frequently in boys as in girls or in male and female and they are very nasty and unpleasant conditions with many recurrences. And finally, and I think this is an important point, if you wish to eradicate these types of infections then we need or should do it. If you wish to do it in the foreseeable period of time then we should vaccinate both genders.

TT: Have your grandchildren been vaccinated against H1N1?

HH: Yes. Unfortunately, one of my grandchildren acquired it a few days before the vaccine became available in Germany. But he recovered. Everyone else has been vaccinated.

TT: You feel it is absolutely necessary?

HH: Of course it is an important protective aspect. I also consider it as important to be vaccinated in order to avoid further spreading of the flu. Therefore I think that one should really recommend vaccinating a large proportion of the population.

TT: Related to H1N1, bovine spongiform encephalopathy (BSE) or mad cow disease is a highly sensitive issue in Taiwan because of government's recent attempt to lift restrictions on the importation of beef from the US. What are your feelings on this issue?

HH: BSE occurred as an epidemic class in Britain. There were a few cases of BSE outside of Britain and they were mainly due to the consumption of meat, which had been exported from Britain.

The disease is identical to what is called the Jakob-Creutzfeldt disease, which occurs sporadically everywhere at a very low rate. So at this moment I cannot see that there exists a very high risk from BSE transmission from meat imported from other countries creating real risk for the population.

The epidemic occurrence of this type of mad cow disease in humans — so far it hasn't happened — even in Britain it didn't happen. There were a couple of cases, of course, small classes of cases, but the feared effects that were initially anticipated didn't come in. We are still not fully out of the situation because of the very long latency period but at least at the moment it doesn't look so that this will be a real threat to the population.

TT: You've had a long career — what is the single greatest advancement, whether technological or scientific for cancer research.

HH: It's very difficult to say. If you look at this from a general viewpoint it's very hard to pinpoint an individual event sticking out completely.

If you look into cancer treatment, which is itself an important aspect, a number of advancements have been made particularly as far as ... childhood cancer is concerned. Leukemia and Hodgkin's disease are both success stories. Also radiotherapy has improved quite substantially and chemotherapy treatments.

As far as prevention is concerned, I think the development of vaccines against the hepatitis B virus and prevention of liver cancer — particularly in this region of the world.

TT: Yes, I understand that the public health system in Taiwan made many advances in this field.

(In the 1980s hepatitis B infected one out of every six children born in Taiwan and was responsible for killing an average of three people every day due to liver cancer and cirrhosis caused by the virus. In 1984, Taiwan became the first country to vaccinate every newborn against hepatitis B. According to the Department of Health, the immunization policy reduced the prevalence of the disease over the past two decades from 17 percent to 1.7 percent of the population.)

HH: This is of great importance and Taiwan played a pioneering role in this whole story. There is no doubt about it. So of course we hope HPV is coming into the same frame. It is also highly preventable. We still need to identify more risk factors and try to better understand the risks arising from them in order to develop better means to prevent other types of cancers. But I think the chances are good. Diagnostic procedures have of course improved.

TT: But it seems that the relationship between viruses and the roles they play in cancer are increasingly recognized.

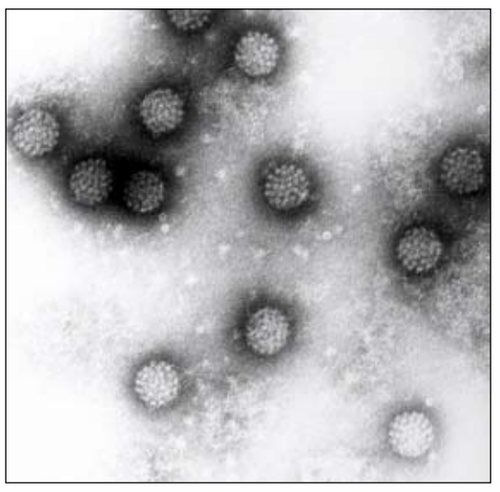
HH: It will be important and it hasn't been recognized in the past. We calculate now that 21 percent of global cancers are linked to infections. If you take it from a global scale, not on the individual country scale, you can say that the infections are by now the, how should I say it, the most important risk factor for cancer — even exceeding smoking. If you take smoking on a global scale it's about 18 percent of cancers. In individual countries the individual percentages are much higher, for smoking. So in a way, that is something that is indeed new and it is important for prevention in particular right now.

TT: What are the necessary conditions for burgeoning scientists to pursue and provide contributions to the field of science.

HH: Well, I guess it is excellent training in the field. Also, young people should have sufficient free space to develop themselves. If they try to create original ideas, [they] are not immediately blocked by the advisors because it doesn't fit into the respective area.

There is one point that I find extremely important: They have to have a certain period of time — say two or three years — where they should not be under this enormous pressure to publish papers but first of all to become acquainted with a certain area and be able to do original work. The final point is that they should not believe in dogmas. [They should be] non-dogmatic.

This interview has been condensed and edited.



This photo made available by the German Cancer Research Center shows an electron microscope image of human papilloma viruses. PHOTO: EPA