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"Difficult to translate data without basic research"

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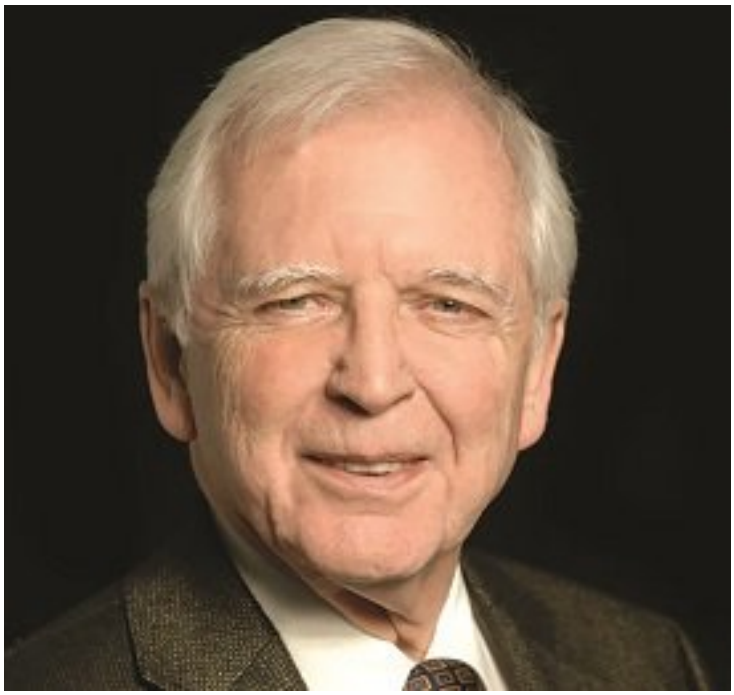
Difficult to translate data without basic research



Singapore:Ã?Â It took decades of success, frustration and achievements for Prof. zur Hausen to identify the viruses that caused cervical cancer and subsequently the development of cervical cancer vaccines. The cervical cancer vaccine market is expected to grow from $1.8 billion in 2001 to $2.2 billion by 2018.

During his visit to Singapore to be a part of the Global Young Scientists Summit 2015, Prof. Harald zur Hausen spoke to *BioSpectrum Asia* about his journey in studies of epidemiology and the role of viruses in certain cancer development.

How did you end up studying viruses causing cervical cancer? Was it your area of interest or did you accidentally come across this significant research?

I have been working on viruses for 55 years now. I always desired to do medically inclined research during my student time and maintained the interest throughout the years. For 20 years, I was the scientific director of a German cancer research center and during that time, I used to do a lot of work on cancer development and also some of the technical developments in cancer.

I became aware of the fact that bacteria could be infected by bacterial viruses and they acquire new properties because of the uptake of some foreign materials. This triggered the idea that we might have some chronic diseases caused by viral infection. We might have similar trait or link in human occurring diseases. This was indeed the basis of my studying medicine and later starting to work on a question that extended to the contribution of infection to cause human cancer, particularly to malignant as well as non-malignant chronic diseases.

What was the basis of your research? Was it a hypothesis that cervical cancer is caused by virus or you concluded it in later years of research?

I started studying the role of viruses causing human disease, particularly cancer, in 1962. So it has been a long period. It was a hypothesis based on the fact that existing epidemiological data supported that cervical cancer is linked to sexual contact and in the past century the link between early transmissions of bacterial infection, in particular to cervical cancer have been studied. At the end of the 60s, two studies were going on to demonstrate that HPV, the so called general form of HPV, is responsible for cervical cancer. I speculated that due to the fact that genital warts occasionally convert into malignant tumors and I knew that papilloma virus is a cause of genital warts, I presumed that this virus might cause cancer in the cervix. So we started working actively on this question in 1972. We came across the fact very quickly. What had been assumed lately that there exists only one virus to cause the disease is wrong. In fact, we realized that it takes multitude of different viruses to cause cervical cancer. We tried extensively to isolate the virus from genital warts and it took us seven years, from 1972-79, to accomplish the isolation process.

We came up with some preparation and derived a methodology which permitted us to work on that virus and clone the DNA and characterize it, which is now called HPV 6. We were first disappointed as we could not find any link to cervical cancer but managed to isolate another virus which was relatively closely related to HPV 6, which is now called HPV 11. This HPV 11, under certain conditions, exhibited latency to other types of agents which we were able to identify in a specific type of technical set up and indicated similarity to the nature observed in the biopsy of cervical cancer. They were related but not identical.

Two of my students were tasked to clone it, label it and analyze it and after we were successful we were able to characterize HPV 16 and HPV 18. We concluded that HPV 16 and HPV 18 are linked to most cases of cervical cancer. It was quite clear that they were important because it demonstrated quickly that they are integrated into our DNA and expressed gene mutation that caused cervical cancer.

What was the response of pharmaceutical companies in translating the research into cervical cancer vaccines?

In 1984, we talked to a number of pharmaceutical companies to sponsor a joint program in the development of vaccines against these viruses which had been remarkably unsuccessful till then. However, only one pharma company was initially interested and started to sponsor the program. The company was later acquired and the decision makers of the new company did not support the vaccine program on the basis of their analysis that there would be no market for these vaccines in future. The program was halted and we were left to frustration.

At the end of 1980s some US-based companies took interest. The first company to take interest was Merck Sharp and Dohme and the second was a biotech company, MedImmune. It was an extremely successful vaccine and today several hundered million doses of vaccines are produced. The rate of side effect can be calculated as one in one hundred thousand.

It was a long story with elements of success, achievements and frustration. Reaching the application stage spanned over a number of years, from 1982 to 2006 and today many countries like Australia have implemented it very effectively for the prevention of cervical cancer.

If cervical cancer can be caused by viruses, does it mean that other cancers could also be linked to viral infections?

In the 1980s and in parts of 1990s, we were focusing on understating the mechanism of how malignant tumors arise and we studied additional mutational events necessary for the research. In that period of time, I also started to look at any other infection that could be caused by this virus. This was particularly intensive after 2000 when we started working on a different group of viruses. At this moment, we can roughly calculate that 20 percent of global cancer incidences is linked to infection. It means it may not directly be the cause of cancer but somewhere related to the growth of cancer cells.

Can you highlight some of other cancers linked to virus or an external element?
For instance, we studied and derived the link of our nutritional habits to cancer such as colon cancer. We became very interested in this study over different geographies and concluded that non-beef consuming countries like India had low instances of colon cancer.

Based on large global data, I felt that consumption of certain type of red meat like beef may be the cause of certain cancers in the human body. This hypothesis directed us to isolate the virus from cattle blood, assuming that if there is something in blood

component, it would be in red meat also. Amazingly enough, we soon came across number of agents which had not being categorized before from the blood of cattle. I did geography wide research on pattern of colon cancer based on meat consumption and travelled to different countries.

We were successful in finding some evidence that the presence of infectious agents in humans is linked to specific types of cancer. Data seemed to indicate that an infection could be acquired by external factors and subsequently developed by the immune reaction.

Another interesting aspect was the geographic data of breast cancer which is also a high risk area. There were few remarkable exceptions in the studies. We realized that India has higher incidents of breast cancer than colon cancer. In Japan and Korea, the rate of colon cancer went steep after 20 years of Second World War and Korea war, respectively. It suggested that there is a certain pattern in geographic occurrence of colon cancer and breast cancer. We analyzed that dairy products play a certain role in the rise of cancer, particularly milk consumption and as the milk consumption in countries like India, China and Mongolia went up, the rate of certain cancers like breast cancer also increased. Also, the meat factor led to colon cancer, derived from the same type of species. Interestingly, I studied that in certain parts of India where beef consumption is prevalent has instances of colon cancer, which is uncommon in the rest of the country.

Another interesting study from a Swiss research center indicates that lactose deficient people are more protected from breast cancer and also lung infections, which is still unexplained. So, we see this study as quite a support for breast cancer as there is the involvement of the milk factor.

How do you see the awareness in different geographies of Asia regarding prevention of cervical cancer?

The awareness level is different in different countries. In Indonesia, there is no awareness program whereas Japan started only in 2014. Even China has not been active in preventing cervical cancer. Only some countries of Asia, like Australia and Singapore, have mandated cervical cancer vaccination. We need to educate people and physicians for the prevention and occurrence of cancer.

Do you feel some countries are ignoring basic research? Are pharma companies in too much of a hurry to pursue translational research?

Translation of research is speeding up and some part of the world has been ignoring basic research. If there is no basic research, it would be difficult to translate data into a new research. Politically, it would not be prudent to not invest in basic research and only translational research. Basic research is mandatory even for poor countries, at least for some areas of disease. Taiwan has been very interested in basic research to derive applied research, for instance, on the study of liver diseases and they have been successful in bringing game changer research in this area.

Pharma companies do their own research but they look for profits in the future. We need more application oriented research but we need basic research as well.

What are the changes you see in the way research projects are pursued nowadays?
Researchers today are in a much more difficult situation because they are under pressure to derive conclusions quickly. Some disease areas are heavily funded whereas some are sidelined or completely ignored. We are so directed towards one direction that we might ignore some potential and much needed areas. This is a grave error in scientific research. Researchers need to have a playground for novel ideas and to look into areas that are neglected.

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