Europe Medical

An Interview with Harald zur Hausen

Born in 1936, Harald zur Hausen completed undergraduate and medical studies in his native Germany. He moved to Philadelphia for a three-year fellowship in molecular biology, studying how viruses induce chromosomal breaks. Upon returning to Germany, Dr. zur Hausen turned his attention to the idea that viruses might cause cervical cancer. He focused on the role of sexually transmitted viruses, in part inspired by an 1842 report noting that cervical cancer is absent among nuns. In 1983, he published a study linking cervical cancer to infection with certain types of human papilloma virus (HPV). This discovery provided the basis for the HPV vaccine, which can prevent cervical cancer as well as certain oral cancers in both men and women. In 2008, Dr. zur Hausen was honored as a recipient of the Nobel Prize in Physiology or Medicine.

Why as a young doctor did you set out to study the role of viruses in cancer?

During my medical training, I became aware of data on bacterial phages, showing that the phages left their genomes in the bacteria they infected and may have changed the properties of the bacteria. This triggered the idea that cancer might be the same kind of story: Normal cells would pick up a viral genome, and the viral genome would persist and subsequently contribute to the development of cancer. A little bit of a naïve idea, but it followed me through the more than 50 years of my career.

Your model and your findings proved correct, but met with resistance along the way. Tell us a bit about that.

At the end of the 1960s the idea came up that the herpes simplex type 2 virus could play a role in cervical cancer. So we started to look in cervical cancer biopsies and tested close to 100 of them. Not in a single one was there any herpes simplex virus type 2 DNA. At a meeting in 1974, a well-known researcher claimed to have found a piece of herpes simplex type 2 DNA in one cervical cancer biopsy. I presented our work at the same meeting. Because I was supposed to be a medically trained person without a background in molecular biology, as some of the colleagues claimed, they simply didn't believe our negative results. I must say that meeting was, for me, the worst professional experience I ever had, even later in my life.

How did the work on human papillomavirus (HPV) begin?

I came across a review on papillomavirus that described how papillomas, including genital warts, develop. I also found studies showing that genital warts occasionally converted to malignant tumors. That fascinated me. We initiated studies isolating viral DNA from individual warts. It took us about seven years before we had a specimen from which we could isolate sufficient DNA to use for labeling procedures. We saw that papillomavirus is indeed present in many genital warts, but to our disappointment we didn't find the genital wart virus in cervical cancer. However, using this material enabled us to isolate a related virus, which we named HPV-11.

What was the path from this finding to the breakthrough?

Using HPV-11 DNA as a probe against biopsy material from cervical cancer, we saw a very faint signal in samples from a few tumors. That triggered the idea that there should be something not identical, but related, in those tumors. At that time I had several skillful students and co-workers in the lab. They quite quickly isolated DNA for HPV-16, which, it turns out, is found in 50% of all cervical cancer biopsies, and a bit later HPV-18, for which 20% of biopsies are positive. The papers were published in 1983 and 1984, the vaccine was licensed in 2006, and by now many millions of young people have been immunized.

Looking back on your training and career, do you have any advice for our students?

Many talented young people stay in the same field as their mentors, a bit of scientific inbreeding. Look into other areas to see whether there is something which would fascinate you even more, using the expertise that you have. Also, learn to be critical and not to trust all the dogmas. Currently, for example, we are investigating whether single-stranded DNA viruses that we have isolated from cattle might contribute to the increased risk of colon cancer associated with consumption of red meat.

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Computer model of HPV