Therapeutic cancer vaccines

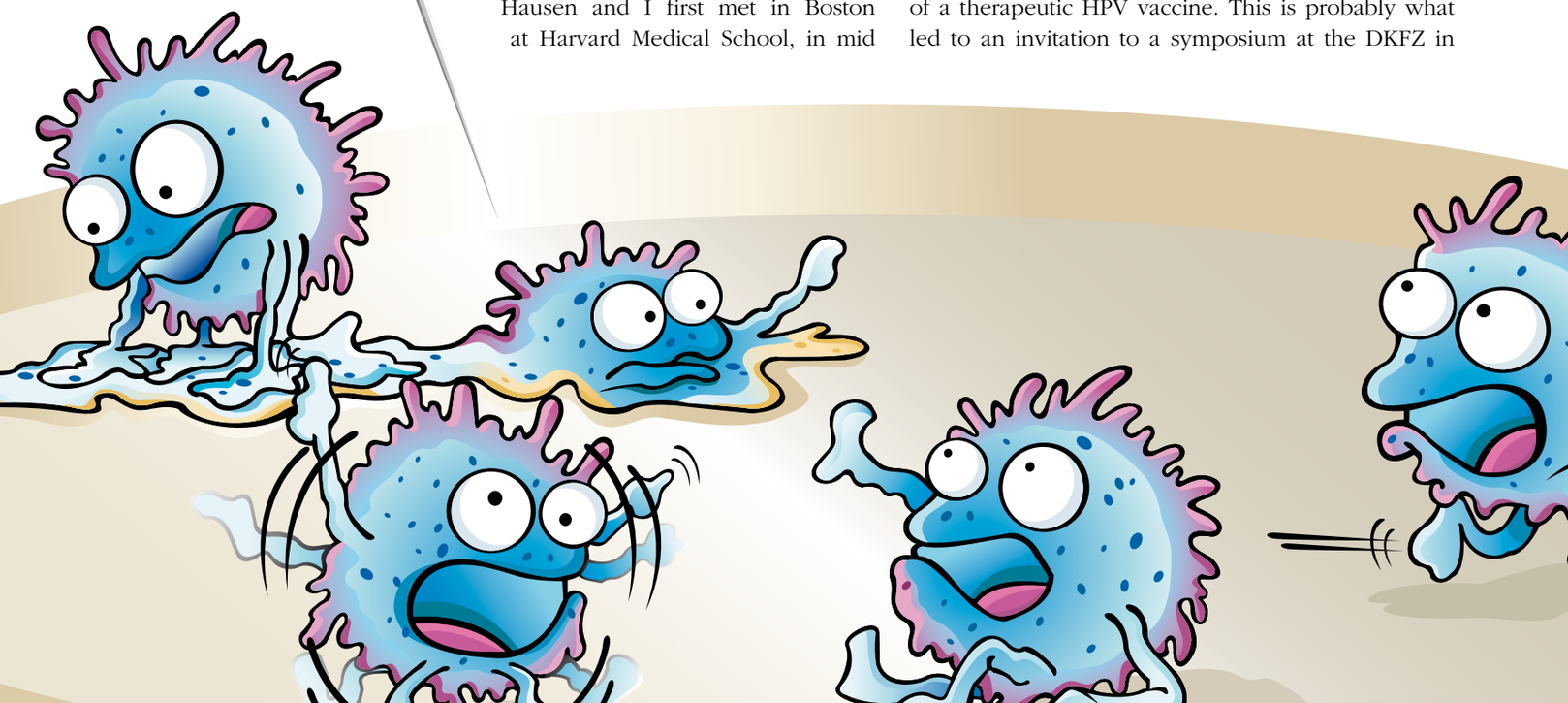
Vaccines against virally induced tumours

When Prof. Dr. Harald zur Hausen was awarded the Nobel Prize for Medicine, in 2008, Dr. Manfred Lautenschläger spontaneously offered to support the scientific work of the Nobel Prize winner by establishing a research team. This funding – one million Euros over four years – is now beneficial for PD Dr. Dr. Angelika Riemer: the young scientist wants to push the development of a vaccine at the German Cancer Research Center (DKFZ), which aims at healing even already existing infections with the cancer-producing Human Papilloma Virus (HPV).

Masiar Sabok Sir spoke with the ambitious researcher for labor&more.

Dear Dr. Dr. Riemer, in February of this year you received Prof. zur Hausen's offer to establish your junior research group "Immunotherapy and -prevention" at the DKFZ. What were your thoughts at this time and how did this come about?

Angelika Riemer: At first I was naturally a little speechless. Prof. zur Hausen and I first met in Boston at Harvard Medical School, in mid 2008, so this was before he was awarded the Nobel Prize. Back then Prof. zur Hausen received an award from a Harvard Foundation and held a lecture on the subject. You don't often get the chance to meet the founder of your research area so of course I attended. At the end of his lecture I felt the need to introduce myself to him. It was simply an honour for me to meet him. At the next conference we spoke in more detail about my research, since I am working on the basis of a therapeutic HPV vaccine. This is probably what led to an invitation to a symposium at the DKFZ in

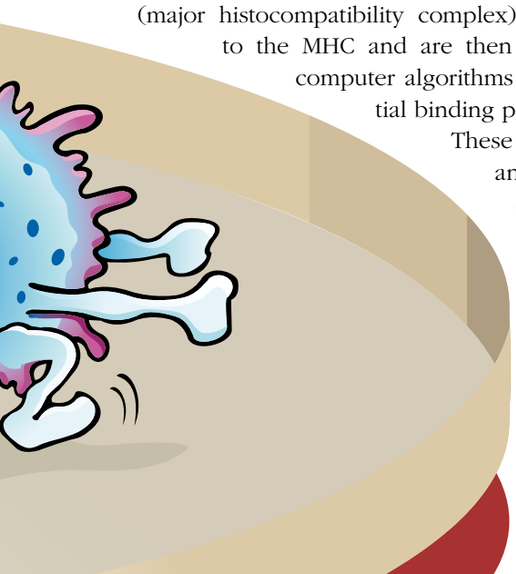


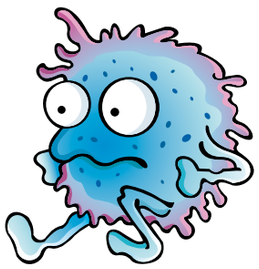
Angelika Riemer studied medicine at the University of Vienna, Austria (with exchange semesters in Australia and England) and graduated in 2002 with a doctorate in medicine (Dr. med. univ.). Thereafter she began a doctorate programme in molecular biology and, in 2005, received a doctorate in natural sciences (Dr. rer. nat). In 2007 Angelika Riemer qualified as a professor in immunology with the professorial dissertation "From passive to active tumour immunotherapy: Mimotope vaccination for epitope-specific induction of trastuzumab-like anti-Her-2 antibodies". After a stay as a postdoctoral research fellow at the Dana-Farber Cancer Institute/Harvard Medical School in Boston (2008–2009), she completed the specialist doctoral training in immunology. Since July 2010, Angelika Riemer is head of the junior research group "Immunotherapy and -prevention" at the DKFZ in Heidelberg.

Heidelberg in February. It was there that he told me about the one million Euro being made available by the Lautenschläger-Foundation on the occasion of the Nobel Prize for the establishment of a new group, and that he was allowed to select the group leader. He asked me if I was interested.

What are the goals of your junior research group that was founded in July, and what are your research findings to date?

The main goal is the development of a therapeutic HPV vaccine. HPV is an ideal test-case for the development of cancer vaccines because with all other types of cancer one actually always has the same problem: tumour antigens are self-antigens. With HPV-induced tumours one is so to say "lucky" in that the tumour antigens are viral antigens, against which it is much simpler to induce an immune response. This is why the prophylactic vaccine is so successful, because it can prevent the infection. But it can only help persons who have not yet come in contact with the virus, and therefore should, if possible, be given to children. If the virus is already present inside the cells, antibodies do not help because they cannot reach it anymore. In this case one needs a vaccine that can induce a cellular immune response. Our approach is that using mass spectrometry we want to directly demonstrate which viral epitopes are actually present on the target cells. To do so, an immunoprecipitation is carried out first. During the immunoprecipitation, peptides presented by MHC-Class-I (major histocompatibility complex) molecules remain bound to the MHC and are then eluted. At the same time computer algorithms are used to predict potential binding peptides for each MHC type. These are synthetically produced and mass spectrometry reference spectra are created. Statistical methods are then applied to examine whether or not a reference spectrum is present in the eluted spectrum.





If yes, one can conclude that this peptide is actually present on the cell surface.

What would be the next step?

Up to now epitopes have usually only been identified for the most common MHC type. Such a vaccine could only be given to people with exactly this MHCtype. With regard to a universally applicable therapeutic vaccine we aim to include epitopes for multiple MHC types, so-called supertypes, so that together over 95% of the population is covered. But it is still a very long way to vaccine formulation. The next goal is epitope identification for the various MHC types.

Which types of cancer is HPV responsible for?

HPV can trigger various types of cancer. Mostly it is presented as a female problem, but that is not even half the truth. Of course, cervical cancer is the most common HPV-induced cancer. Basically however all mucous membranes in this area can be infected and transformed by HPV, i.e. also the anal area – or it can cause penile carcinomas. What is becoming more and more common are HPV-induced cancers in the oropharynx. Especially the tonsils are susceptible. HPV-induced cancers are nowadays considered to be a new subgroup of HNSCC (head and neck squamous cell carcinoma). This is of course the case in both sexes.

Would it not be sensible in this context to vaccinate men as well as women?

That would definitely be sensible, particularly with a view to eradicating the virus. It is simply a question of costs. As long as the vaccine is still so expensive, one attempts to protect only those who are most likely to develop a disease.

Which interim conclusion do you come to, after two months, regarding the framework conditions at the DKFZ?

For me this is a tremendous opportunity and challenge, which I intend to use as best as possible. Within the framework of the DKFZ and in the close proximity to other institutions such as, for example, the University of Heidelberg there is something very special in the air. There is a concentration of people who are enthusiastic about something and who want to discover things and make a difference. That makes working here extremely enjoyable and creates the perfect foundation for successful research.

Thank you for the interview and we wish you great success for the future!

Further information can be found at:

→ **www.dkfz.de/de/immuntherapie-immunpraevention/index.html**