

**Black sheep in the family: Why some infections with the Epstein-Barr virus cause cancer**

**Epstein-Barr viruses (EBV) are very common around the world; almost everybody is infected. In most cases, an infection causes no harm, but sometimes the outcome is a serious disease. EBV may lead to infectious mononucleosis (Pfeiffer's disease), which is common in Germany; in other parts of the world it even causes cancer. The reasons that EBV infections take such diverse courses have been unclear. Now scientists from a team headed by Henri-Jacques Delecluse at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have found out that Epstein-Barr viruses come in various strains that differ in terms of their aggressiveness. These findings are extremely important both in finding strategies to fight the diseases caused by EBV and for developing vaccines against infections with the virus.**

Over 90 percent of the world population is infected with the Epstein-Barr virus (EBV). Fortunately, only a fraction of those who are infected actually develop a disease. In most cases, the virus persists unnoticed in the body throughout a person's lifetime – provided that his or her immune system is intact. However, there are cases where it causes various diseases: in Europe and North America, it leads to infectious mononucleosis (Pfeiffer's disease); in Central Africa it causes Burkitt's lymphoma; and nasopharyngeal cancer is a common result in Southeast Asia.

So far, it has been unclear why EBV infections take such diverse courses. In Africa, simultaneous infection with the parasite that causes malaria may induce Burkitt's lymphoma. The age of an initial infection is believed to play a role in infectious mononucleosis, and in China, substances in people's diet seemed to promote nasopharyngeal cancer.

"Scientists have known that there are differences in the genetic material of the various viruses that occur worldwide," says Henri-Jacques Delecluse of the German Cancer Research Center. "We have now been able to show for the first time, with help from colleagues from Zurich, that these genetic differences are actually responsible for the diverging properties that the viruses exhibit in terms of promoting disease."

Delecluse and his coworkers initially isolated viral DNA from two patients: one from North America who suffered from infectious mononucleosis; the other was a man from Hong Kong who suffered from nasopharyngeal cancer. The DKFZ scientists discovered that the two virus strains had important differences: The virus from the Chinese cancer patient is particularly efficient in infecting epithelial cells of the mucous membranes, while that of the American patient suffering from infectious mononucleosis infects only B cells of the immune system.

"Although Epstein-Barr viruses can be found in the epithelial cells of nasopharyngeal carcinomas, researchers have been puzzled by its behavior in the laboratory," Delecluse says. "They haven't been able to infect these cells with EBV, or have had to use tricks to do so. "Now we know that the laboratory strains were completely different from those that were isolated from cancer patients."

Delecluse expects that his findings will be a major step toward preventing virus-induced cancers in the future. "We are currently developing a vaccine based on so-called 'virus-like particles', or VLPs. These are empty virus shells that can prompt the body to mount an immune response." VLPs are already being used successfully in vaccines against human papillomaviruses and hepatitis B viruses. "We previously believed that the Epstein-Barr virus

is one and the same around the world. Now we know that there are different strains; in our efforts to develop vaccines, we should focus on strains that seem to be particularly aggressive.”

Ming-Han Tsai, Ana Raykova, Olaf Klinke, Katharina Bernhardt, Kathrin Gärtner, Carol S. Leung, Karsten Geletneky, Serkan Sertel, Christian Münz, Regina Feederle and Henri-Jacques Delecluse: Spontaneous lytic replication and epitheliotropism define an Epstein-Barr virus strain found in carcinomas. Cell Reports, DOI: 10.1016/j.celrep.2013.09.012

A picture for this press release is available on the Internet at:  
[www.dkfz.de/de/presse/pressemitteilungen/2013/images/epstein-barr-virus.jpg](http://www.dkfz.de/de/presse/pressemitteilungen/2013/images/epstein-barr-virus.jpg)

Caption:

Electron micrograph picture of Epstein-Barr viruses

The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) with its more than 2,500 employees is the largest biomedical research institute in Germany. At DKFZ, more than 1,000 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. The staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. Jointly with Heidelberg University Hospital, DKFZ has established the National Center for Tumor Diseases (NCT) Heidelberg, where promising approaches from cancer research are translated into the clinic. In the German Consortium for Translational Cancer Research (DKTK), one of six German Centers for Health Research, DKFZ maintains translational centers at seven university partnering sites. Combining excellent university hospitals with high-profile research at a Helmholtz Center is an important contribution to improving the chances of cancer patients. DKFZ is a member of the Helmholtz Association of National Research Centers, with ninety percent of its funding coming from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg.

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