

## PRESS RELEASE

### New findings on infection with the Epstein-Barr virus

Researchers in Bonn decipher how the human body controls a widespread viral infection

**Bonn, February 19 – The Epstein-Barr virus (EBV) can cause certain types of cancer or autoimmune diseases, but how the body controls this common viral infection is largely unknown. Researchers at the University Hospital Bonn (UKB) and the University of Bonn have now identified genetic and non-genetic factors that help the body fight EBV. To do this, they evaluated genome sequencing data, which is actually intended for characterizing the human genome, in a new way. Using the new technique, they were able to estimate the amount of EBV in the blood and find correlations in large health data sets – for example, an increased viral load in people with HIV infections, but also in smokers. There were also indications of new genes that play key roles in EBV immunity. Their findings have now been published in the renowned journal Nature.**

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Approximately 90 to 95 percent of the global adult population is infected with the Epstein-Barr virus (EBV). EBV infection is a risk factor for various types of cancer, such as Hodgkin's lymphoma (HL), and autoimmune diseases, such as multiple sclerosis (MS). After infection, which commonly occurs in childhood, EBV remains hidden in certain white blood cells, the B memory cells, for life. The virus is usually inactive in these cells and, in this so-called latency phase, evades removal by the immune system. The virus is reactivated spontaneously, but also as a result of stress, and then switches to an active state. "Despite its high relevance, very little is known about how exactly the immune system controls lifelong EBV infection and how this contributes to the development of diseases such as cancer or autoimmune diseases. This is largely due to a lack of suitable data—for example, large population-based studies such as biobanks lack direct measurements of EBV viral load," says corresponding author Prof. Kerstin Ludwig from the Institute of Human Genetics at the UKB, who is also a member of the ImmunoSensation<sup>3</sup> and the Transdisciplinary Research Areas (TRA) "Life and Health" & "Modeling" at the University of Bonn.

#### **A new measure to estimate viral load**

"To overcome these limitations, we established that the amount of EBV in human blood can be estimated using genome sequencing data. Genome sequencing data is actually collected to characterize the human genome – so we have 'repurposed' it a little," says lead author Dr. Axel Schmidt from the Institute of Human Genetics at the UKB. The research team examined genome sequences (GS) from the blood of 486,315 participants in the UK Biobank and 336,123 participants in the All of Us project and found short DNA segments that could be attributed to the EBV genome, so called EBV reads, in 16.2 percent and 21.8 percent of the individuals, respectively. "People in whom such EBV reads are detected have, on average, an increased EBV viral load. We were able to demonstrate this with laboratory tests. Since large biobanks, such as the UK Biobank, have collected genome sequencing data for all participants, we now have a measure with which the EBV viral load can be estimated on a large scale," says Schmidt. "This opens up completely new possibilities for investigating the many questions that still remain on the subject of EBV immunity."

### **Active smoking promotes EBV viral load**

First, the authors investigated which non-genetic factors influence EBV viral load. They were able to show that the number of EBV reads was increased in immunocompromised individuals and also in smokers. Smoking is a risk factor for several EBV-associated diseases, although the underlying mechanisms are largely unknown. "Our data indicate that current smoking in particular increases EBV viral load. Other groups have already shown that current smoking has an influence on the innate immune system. This could therefore be an indication that this interaction also plays a role in EBV control," says Schmidt. Another interesting observation was a correlation between the viral load and the season in which the sample was taken – on average, more EBV sequences were found in winter and fewer in summer.

### **New candidate genes for key roles in EBV immunity**

At the genetic level, the Bonn researchers found a strong association between EBV viral load and the major histocompatibility complex (MHC) locus. This section of our genome contains blueprints for special proteins that help the immune system recognize germs such as viruses or bacteria, making this DNA region a key player in the immune system. In addition to the MHC locus, associations were found in 27 regions of DNA outside the MHC that were largely consistent across both biobanks. Among the genes located in these regions are some with known functions in the immune system that could play a plausible role in controlling EBV viral load, but also a large number of new candidates. Analyses of genetic overlap with EBV-associated diseases also led to new hypotheses regarding the mechanisms involved in MS and identified new diseases for which EBV could be pathophysiologically relevant, such as type 1 diabetes.

Prof. Ludwig sums up: "Our results serve as a basis for understanding EBV immunity, and they also open up avenues for new mechanistic studies and therapeutic approaches for EBV-associated diseases. In a broader sense, our study illustrates how by-products of human genome sequencing data can be used to investigate persistent viral infections."

**Institutions involved:** In addition to the UKB and the University of Bonn, the University of Tokyo in Japan was also involved in the study.

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**Image material:**



**Caption: New findings on infection with the Epstein-Barr virus**

(from left) Axel Schmidt and Kerstin Ludwig are deciphering how the human body keeps a widespread viral infection under control.

**Image credit:** Institute of Human Genetics at UKB / Andreas Stein

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**About the University Hospital Bonn:** As one of Germany's leading university hospitals, Bonn University Hospital (UKB) combines excellence in medical care and research with high-quality teaching. Every year, UKB treats more than half a million outpatients and inpatients. Around 3,500 students are enrolled in medicine and dentistry, and over 600 individuals receive training in healthcare professions annually. With around 9,900 employees, UKB is the third-largest employer in the Bonn/Rhein-Sieg region. In the „Focus hospital rankings“, UKB is rated the top university hospital in North Rhine-Westphalia and has the second-highest case mix index (an indicator of treatment complexity) of all university hospitals nationwide. In 2024, UKB secured nearly €100 million in third-party funding for research, development, and teaching. For the fourth consecutive year, the F.A.Z. Institute recognized UKB as both “Germany's Training Champion” and “Germany's Most Desirable Employer.” For current figures and further information, please refer to the annual report at: [geschaeftsbericht.ukbonn.de](https://geschaeftsbericht.ukbonn.de)