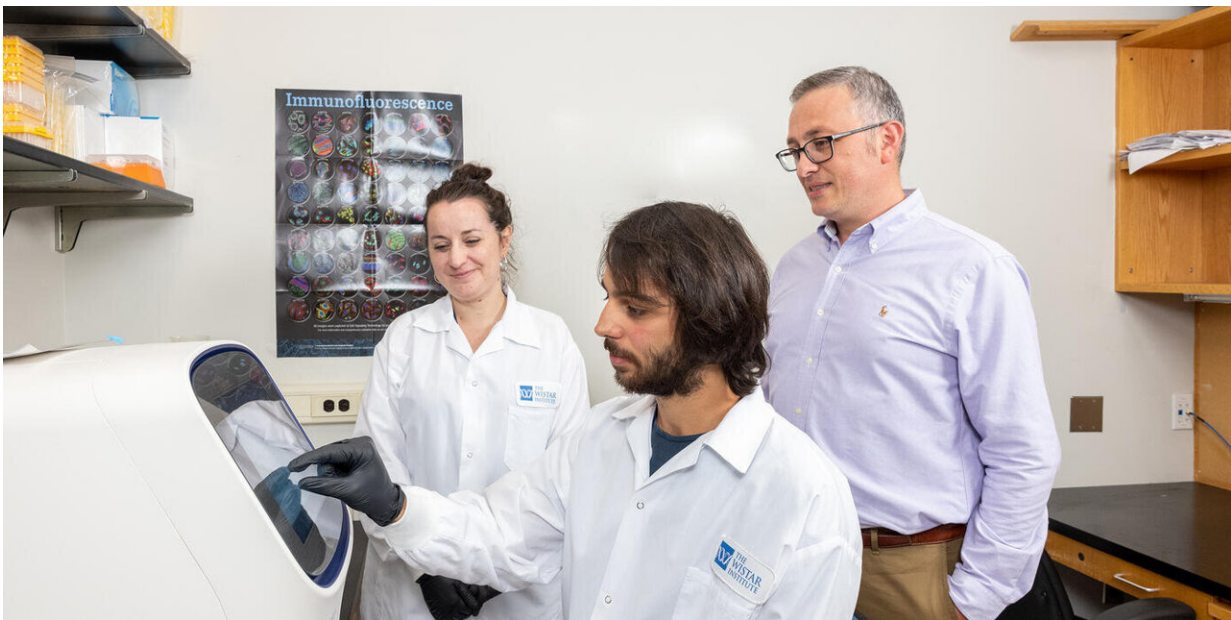


Scientists identify therapeutic target for Epstein-Barr virus

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Credit: The Wistar Institute

A new study by researchers at The Wistar Institute, an international biomedical research leader in cancer, immunology, infectious disease, and vaccine development, has identified a new potential pathway for developing therapeutics that target Epstein-Barr virus (EBV). They discovered that the way the EBV genome folds, and thereby expresses itself and causes disease, is more complex than researchers originally thought, and they identified molecules that could be targeted to disrupt

this folding.

"We identified two cellular proteins that are important to folding the EBV genome." said Italo Tempera, Ph.D., associate professor in the Gene Expression & Regulation Program at The Wistar Institute and corresponding author on the paper. "There are existing drugs that target one of these proteins. And our data suggests that if we use that drug on EBV infected cells, we have a way in which we can actually interfere with the folding. That means we can interfere in the way in which the EBV [viral genome](#) is functioning."

EBV, which affects more than 90 percent of individuals worldwide, is a dynamic virus, meaning that it can change its [gene expression](#). If certain viral genes are expressed, the virus infects B-cells and causes them to overmultiply, which is especially problematic in individuals with suppressed immune systems, such as transplant patients.

Tempera and his colleagues wanted to understand the mechanics behind how the virus manipulates its genetic expression. To do this, they used a modified DNA sequencing technique to examine how the genome folds under different conditions.

"The [virus](#) was clever to use the same machinery that regulates the conformation of the human genome to also regulate its own gene expression," said Tempera. Specifically, the researchers found that EBV uses two proteins, CTCF and PARP1, that also play a role in the expression of the human [genome](#).

PARP1 is already a target of the drug, olaparib (sold under the brand name Lynparza), which is used to treat patients with ovarian cancer. This new study suggests that the drug may have a use for treating EBV positive lymphomas, as well.

"Usually PARP1 is targeted in the context of DNA damage," said Tempera. "Our paper shows that there is another role of PARP1 in the chromatin folding, so this suggests that maybe we can expand the way in which we can use this drug not only to interfere with DNA damage, but we also might interfere with DNA folding and gene expression, which is something that we are testing now in the lab."

More information: Sarah M. Morgan et al, The three-dimensional structure of Epstein-Barr virus genome varies by latency type and is regulated by PARP1 enzymatic activity, *Nature Communications* (2022). [DOI: 10.1038/s41467-021-27894-1](https://doi.org/10.1038/s41467-021-27894-1)

Provided by The Wistar Institute

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