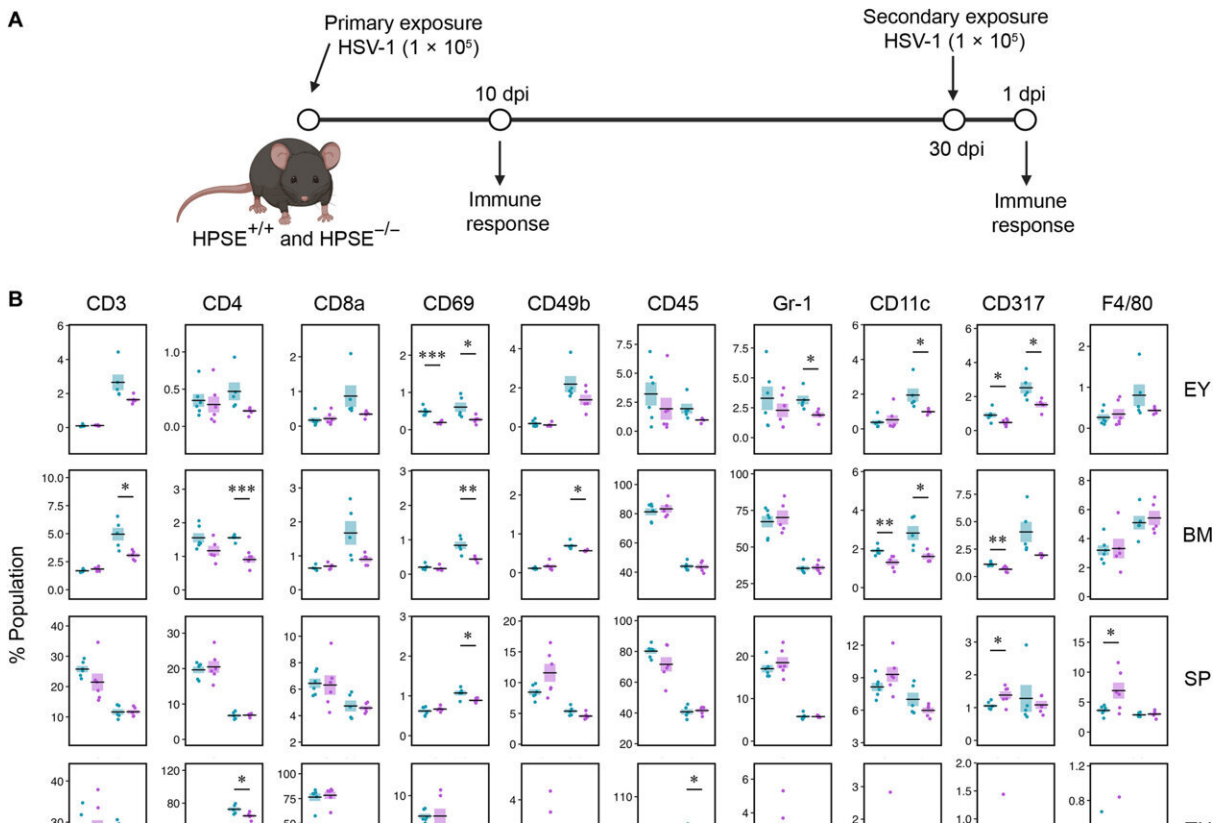
Herpes study adds to understanding of viral reinfections, including how to potentially prevent them

May 1 2023, by Emily Stone



HPSE regulates leukocyte development and tissue trafficking in a murine model of HSV-1 reinfection.(**A**) Proportions of parent populations determined by flow cytometry are represented as median ± SEM after the primary (pri) and secondary (sec) infection (n = 4 to 6 mice per group). Eye tissue (EY) represents the peripheral site of infection, bone marrow (BM) represents a primary lymphoid organ, whereas spleen (SP) and thymus (TH) represent secondary

lymphoid organs. Cell markers represent the following cell types: CD3, CD4, and CD8a: T cell subsets; CD69: lymphocyte activation; CD49b: natural killer cells; CD45: leukocytes; Gr-1: neutrophils and monocytes; CD11c: dendritic cells; CD317: plasmacytoid dendritic cells; F4/80: macrophages. Significance was determined by unpaired two-tailed *t* test with Holm-Sidak correction for multiple comparisons. (**C**) Summary representation of significantly different cell populations in (**B**). Positive effect size (purple) indicates significantly higher cell abundance in $HPSE^{+/+}$ compared to $HPSE^{-/-}$, and negative effect size (green) indicates significantly higher cell abundance in $HPSE^{-/-}$ compared to $HPSE^{+/+}$. (**D**) Graph representing the collection time point of serum from HSV-1–infected mice. (**E**) Graph representing virus-neutralizing ability of serum from 30 dpi. *P P P Science Advances (2023). DOI: 10.1126/sciadv.adf3977

A new study on herpes infections of the eye from University of Illinois Chicago researchers helps shed light on the question of viral reinfections by identifying a key protein involved in viral reinfections that could be targeted by antiviral drugs.

The UIC team examined how the heparanase protein, which is present in all our cells, affects reinfection from the herpes simplex virus type 1 in mice. They found that inhibiting heparanase activity can protect the eyes from being reinfected. Mice that had their heparanase protein blocked showed no signs of cloudiness in their corneas after a second infection, as compared with mice with normal heparanase, whose corneas showed significant signs of reinfection.

Additionally, the researchers found that when the protein is activated due to infection, the immune system may exacerbate the symptoms during a second infection. The study, published recently in *Science Advances*, also discovered that when heparanase is malfunctioning, the virus is more likely to cause disease in individuals previously infected with the virus.

Taken together, the findings suggest that inhibiting the activity of the heparanase protein can be an effective way to prevent herpes simplex virus type 1 reinfection, potentially leading to a breakthrough in preventing the recurrence of these infections.

"We wanted to know if we could better protect them from infection, and we found that we could," explained Chandrashekhar D. Patil, co-lead author on the study, and a visiting scholar in the department of ophthalmology and visual science.

Reducing reinfections is of crucial importance because people infected multiple times with the herpes simplex virus type 1 are at increased risk of health complications, such as an ulcerative disease and even blindness. These findings can also have a significant impact on public health, as they help inform scientists about the possible mechanics of reinfection with other viruses, such as coronavirus. Other research has indicated that heparanase plays a role in COVID-19 reinfections, as well.

While more research is needed to understand the most effective way of inhibiting heparanase to prevent viral reinfections, these findings indicate that blocking the protein could be a promising drug target, explains Deepak Shukla, the Marion Schenk Esq. Professor of Aging Eye Research and the corresponding author of the study.

"This could be the wonder drug down the road," he said. "We could be looking at a broad spectrum antiviral drug."

More information: Rahul K. Suryawanshi et al, Pathophysiology of reinfection by exogenous HSV-1 is driven by heparanase dysfunction, *Science Advances* (2023). DOI: 10.1126/sciadv.adf3977