Research advances potential for test and vaccine for genital and oral herpes

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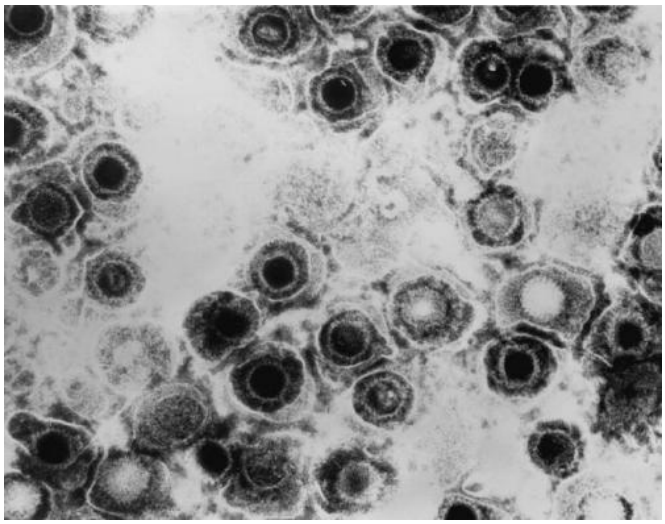

Herpes simplex virus. Credit: CDC

Findings from a pair of new studies could speed up the development of a universally accurate diagnostic test for human herpes simplex viruses (HSV), according to researchers at Johns Hopkins and Harvard universities and the National Institutes of Health (NIH). The work may also lead to the development of a vaccine that protects against the virus.

Depending on the strain and other factors, HSV can cause cold sores—classically associated with HSV1—or genital herpes—classically HSV2—with the latter being the more serious of the two diseases, particularly because studies show that HSV2 makes carriers more susceptible to contracting HIV. Currently, individuals are screened for HSV using a test that distinguishes between a glycoprotein—or a molecule containing a carbohydrate and a protein—present in HSV1, which is common throughout the population, and the considerably rarer HSV2. Whereas the test discriminates between the two variants with high accuracy in the United States and Europe, it largely fails in Africa, where rates of HIV and HSV are highest.

HSV was first genetically sequenced using only European patient strains, and the resulting diagnostic test was developed to identify sequences common to those strains. Scientists have long suspected that the glycoproteins present in African patients who are HSV-positive might differ from patients in the U.S. and Europe.

"Because HSV2 enhances HIV transmission, we have been testing people across East Africa for genital herpes, but everybody was coming up positive. The test was just not as specific as it should be," says Thomas Quinn, M.D., professor of medicine at the Johns Hopkins University School of Medicine and associate director of international research and senior investigator in the Division of Intramural Research at NIH's National Institute of Allergy and Infectious Diseases.

Quinn, who has been conducting research in East Africa for 30 years, was a senior author on both studies, which will appear in print in the August issue of the *Journal of Virology*.

To test the possibility that the glycoproteins differ in African patients, Quinn and his colleagues conducted a series of studies, one characterizing the entire HSV2 genome and another focusing on the glycoproteins present in HSV2 compared to HSV1, the target of several vaccines currently in research and development.

The team collected and analyzed 34 HSV2 strains in Uganda, South Africa, Japan and the United States. They also added two South African sequences gathered by David Knipe, a herpes researcher at Harvard University.

In the first published paper, the team reported that compared to HSV1, HSV2 has less genetic diversity. Besides providing clues to how the two

strains evolved, the findings also have implications for vaccine development, Quinn says, because HSV2's low genetic diversity means fewer antigens could be enough for developing a globally effective HSV2 vaccine.

In the second paper, the team looked more closely at what might be needed to develop a more universally accurate diagnostic test, Quinn says. Because the current test discriminates between HSV1 and HSV2 by looking at variations in a localized region of so-called glycoprotein G, the team focused on the glycoproteins present in HSV by comparing the 36 HSV2 strains from the first paper to 26 previously sequenced strains of HSV1 and looking at geographic diversity among the HSV2 glycoprotein sequences.

According to Quinn, they found that the African strains of glycoprotein G differed slightly from those in strains from other countries. Glycoproteins I and E also showed some variation.

"That explains why the diagnostic test didn't work optimally in Africa," Quinn says, adding that it should now be possible to develop a more universal screening tool. "From this study, you then can make a consensus sequence that is common across the world for HSV2 glycoprotein that is different for HSV1 so you don't get this misdiagnosis."

Provided by Johns Hopkins University School of Medicine