Researchers discover byproducts from bacteria in gum disease can awaken dormant T-cells and HIV viruses

January 5 2015

Dental and medical researchers from Case Western Reserve University found another reason to treat periodontal disease as soon as possible.

They discovered that byproducts of bacteria in gum disease, called metabolic small chain fatty acid (SCFA), can work together to wake up HIV in dormant T-cells and cause the virus to replicate.

Their findings help explain why people with the HIV -infections and periodontal disease have higher levels of the virus in their saliva than HIV patients with healthy gums.

The researchers speculate that byproducts from other bacteria infections in other diseases might change gene expression using similar mechanisms.

For dental patients with HIV, their findings further support how important it is to treat bacterial infections in gum disease early.

This interaction by SCFA and T-cells surprised co-investigators Fengchun Ye, assistant professor of biological sciences at the Case Western Reserve University School of Dental Medicine, and Jonathan Karn, director of the Center for Aids Research and professor and chair of the Department of Molecular Biology and Microbiology at Case Western Reserve's medical school.

Their findings are described in the article, "Short chain fatty acids potently induce latent HIV-1 in T-cells by activating P-TEFb and multiple histone modifications," published in January 2015 in the journal *Virology*.

In the interaction between gum disease and HIV, five SCFA byproducts from two prevalent oral bacteria—*Porphyromonas gingivalis* (Pg) and *Fusobacterium nucleatum* (Fn)—are involved in activating resting immune T-cells carrying latent (inactive) HIV-1 virus.

The process acts much like the jumper cables attached to a live battery recharging a dead one to get it running again, according the researchers.

Ye explained that all humans have a reservoir of resting T-cells that wake up and respond to inflammation to ward off an infection in the body.

"As long as someone is healthy, the reservoir remains untapped," he said.

But for people with HIV, these T-cells can also have the sleeper HIV-1 virus, which remains in a dormant state until awakened, Karn said.

Last year, Ye and Karn discovered that one SCFA—butyric acid—induced a chain of events that reactivate the virus associated with Kaposi's sarcoma, the most common malignancy in HIV patients.

Following that discovery, the researchers expanded their investigation to all SCFAs. They found that a high quantity of butyric acid activates the T-cell and incites virus replication. But smaller amounts of the five SCFA, working together, have the same impact.

"Looking at only butyric acid was misleading," said Karn, the Reinberger Professor of Molecular Biology. "It surprised us to find they all work as

an aggregate."

The impact on waking up T-cells and activating HIV replication was a "double whammy" find that contributes to understanding the little-known microbiome in HIV disease, Karn said.

That prompted the researchers to investigate the mechanism that drives the replication of the virus in gum disease.

HIV antiviral therapy prevents active HIV cells from replicating and doesn't affect the quiet viruses in sleeping T-cells.

As long as the patient is free of gum disease, the virus sleeps and remains in check, Karn said.

More information: Das B, et al. *Virology*. 2015 Jan 1;474:65-81. DOI: 10.1016/j.virol.2014.10.033 . Epub 2014 Nov 14. www.sciencedirect.com/science/ … ii/S0042682214004905

Provided by Case Western Reserve University