Gammaherpesviruses linked to tumors in macaques with simian immunodeficiency virus

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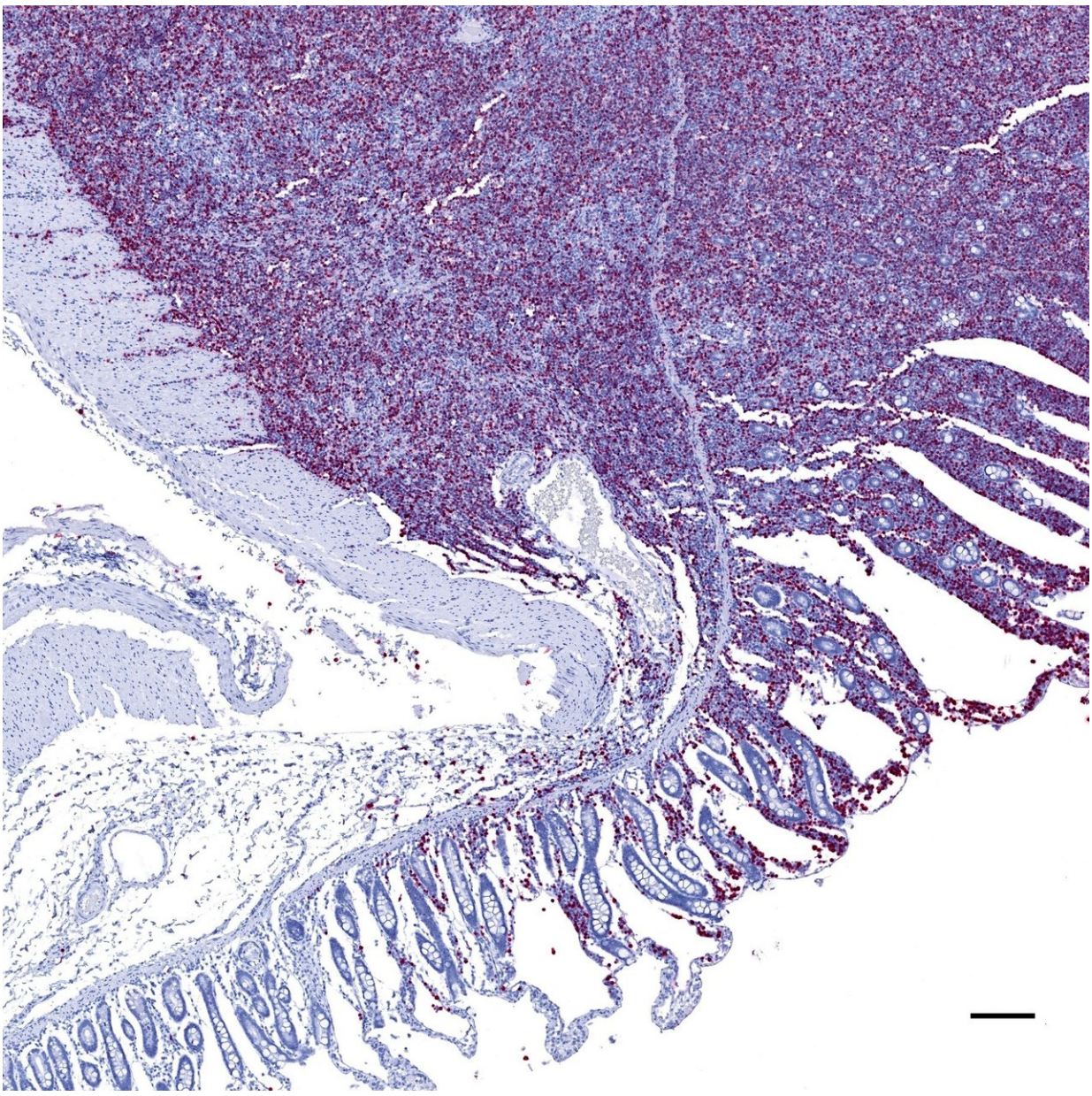

Rhesus lymphocryptovirus (RLCV) detection, using net generation in situ hybridization RNAscope (in red), in jejunum mass classified as Diffuse Large B-cell Lymphoma (DLBCL) in SIV infected Rhesus macaque. Scale bar 100μm. Credit: Whitby et al (2018)

Viruses known as gammaherpesviruses may raise the risk of cancer in macaques infected with Simian Immunodeficiency Virus or Simian Human Immunodeficiency Virus (SIV/SHIV), according to new research published by Vickie Marshall of the Frederick National Laboratory for Cancer Research, Maryland, and colleagues.

In humans infected with HIV, the gammaherpesviruses known as Epstein Barr Virus (EBV) and Kaposi's Sarcoma-Associated Herpesvirus (KSHV) are associated with development of lymphomas and other cancer types. Macaques used in research as animal models of HIV infection can also experience gammaherpesvirus infection, but the role of these viruses in cancer development in the animals is poorly understood.

To help clarify this role, Marshall and colleagues developed new techniques to test for gammaherpesvirus DNA in tumor samples from 18 macaques that were infected with SIV/SHIV from 2001 to 2015 as part of studies conducted by the national laboratory's AIDS and Cancer Virus Program. They compared these results with samples of healthy, non-tumor tissue from the same animals, as well as samples from 32 SIV/SHIV-infected macaques that did not develop tumors.

The researchers found at least one rhesus gammaherpesvirus in all but one of the tumors they studied. In most of the tumors, one of the three

rhesus gammaherpesviruses—known as RRV, RFHV, and RLCV—was predominant and was present in significantly larger amounts than in nearby non-tumor tissue.

Analysis of viral DNA in blood samples from all 40 animals showed that RLCV was associated with cancer risk. Blood samples taken periodically between SIV infection and death revealed different patterns of gammaherpesvirus abundance in healthy animals versus those with tumors. In all of the animals, RFHV levels increased slightly over time, but in those with tumors, RLCV and RRV levels increased significantly and continued increasing over time, while levels flattened in the healthy macaques.

While these results do not confirm whether gammaherpesviruses directly cause cancer in SIV/SHIV-infected macaques, they strongly suggest that the viruses contribute to tumor development in the animals. Since these tumors have characteristics in common with HIV-associated tumors, further study of gammaherpesviruses in SIV/SHIV-infected macaques could help improve understanding of HIV-associated tumors and potential new treatment approaches.

"Cancer caused by oncogenic viruses are a substantial cause of morbidity and mortality worldwide especially in people living with HIV," said lead author Denise Whitby, Ph.D. "Our study emphasizes the utility of non-human primates naturally infected by gammaherpesviruses and experimentally infected by SIV as a tool to study the pathogenesis and potentially treatment of such cancers".

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