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Primate research center plays key role in HIV study in Nature

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In a study reported in *Nature* this month, Yerkes National Primate Research Center researchers were key in determining that treating SIV-infected rhesus macaques with type 1 interferon, a protein known to trigger antiviral responses and inflammation, can have beneficial and detrimental effects on the development of disease.

The Yerkes researchers used high-tech RNA-sequencing technology to study genome-wide expression (transcriptome) of antiviral responses in monkey tissues during various stages of the study. This work was critical to determining that blocking interferon at the onset of infection may be a viable strategy for treating HIV-related disease, but equally important is giving consideration to the viral status of each patient because interferon blockade may trigger a rebound in virus levels in chronic infection.

Steve Bosinger, PhD, a Yerkes researcher, co-director of the Yerkes Nonhuman Primate Genomics Core and a study co-author, says, "Using genomic technology was critical to the study because the interferon system works by inducing hundreds of different antiviral genes. Genomics, rather than single-gene approaches, is needed to adequately assess the viability of the treatment blockade. Using genomics allowed us to identify novel pathways that were perturbed by blocking interferon signaling."

To do this, the researchers used a new version of the rhesus macaque genome that has three times the number of annotated genes than what has been available.

Interferon is the central, crucial component of an innate immune response against viruses. Most viral infections are cleared or are controlled in a few weeks and the interferon response stops. In HIV/SIV, however, the infection persists indefinitely, and the interferon response goes on as well. Because of this, scientists have speculated for years that interferon itself may be a significant contributor to disease in people infected with HIV. In the Nature study, the researchers tested this directly by giving interferon to one group of monkeys and administering an inhibitor in a second group of animals.

The study's lead authors are Daniel Douek, MD, PhD, Human Immunology Section, Vaccine Research Center, National Institute of Allergy and Infectious Disease, and Netanya Sandler, MD, Division of Infectious Diseases, Department of Internal Medicine, University of Texas Medical Branch at Galveston. Robert Norgren, PhD, Department of Genetics, Cell Biology and Anatomy, University of Nebraska Medical Center, provided the rhesus genome reference. Greg Tharp, Msc, a bioinformaticist in the Yerkes Nonhuman Primate Genomics Core, also contributed to the study. Bosinger says the Yerkes Core will perform the genomics components of Douek's follow-up studies, which will examine the effect of interferon blockade on chronic infection and in animals receiving anti-retroviral therapy.

Provided by Emory University

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