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HIV-Like Virus Eliminated from the Genomes of Primates; Excision BioTherapeutics Advancing the Innovation to Clinical Development

Study published in Nature Communications marks a critical step toward the development of a possible cure for human HIV infection

San Francisco, CA, Nov. 30, 2020 (GLOBE NEWSWIRE) -- Taking a major step forward in HIV research, scientists at the Lewis Katz School of Medicine at Temple University have successfully edited SIV – a virus closely related to HIV, the cause of AIDS – from the genomes of non-human primates. The breakthrough, reported in the journal *Nature Communications*, marks a critical step toward the development of a possible cure for human HIV infection. **Excision BioTherapeutics** holds the exclusive license for commercial application of these advancements as it works on the development and commercialization of advanced gene editing therapeutics for the treatment of life-threatening diseases caused by viruses.

“For the first time, a single inoculation of our CRISPR gene-editing construct, carried by an adeno-associated virus, can edit out the SIV genome from infected cells in rhesus macaque monkeys,” said **Kamel Khalili, PhD**, Laura H. Carnell Professor and Chair of the Department of Neuroscience, Director of the Center for Neurovirology, and Director of the Comprehensive NeuroAIDS Center at the Lewis Katz School of Medicine at Temple University (LKSOM) and the Co-Founder and Chief Scientific Consultant to Excision.

Of particular significance, the new work shows that the gene-editing construct can reach infected cells and tissues known to be viral reservoirs for SIV and HIV. These reservoirs, which are cells and tissues where the viruses integrate into host DNA cause the virus to emerge as soon as antiretroviral therapy (ART) is stopped.

Dr. Tricia Burdo, Associate Professor and Associate Chair of Education in the Department of Neuroscience at the Lewis Katz School of Medicine at Temple University, and Scientific Advisory Board member to Excision added, “The SIV-infected rhesus macaque model is an ideal large animal model for recapitulating HIV infection in humans.”

For the new study, the researchers began by designing an SIV-specific CRISPR-Cas9 gene-editing construct. Experiments in cell culture confirmed that the editing tool cleaved integrated SIV DNA at the correct location from host cell DNA, with limited risk of potentially harmful gene editing at off-target sites. The research team then packaged the construct into an adeno-associated virus 9 (AAV9) carrier, which could be injected intravenously into SIV-infected animals. Analyses showed that in AAV9-CRISPR-Cas9-treated macaques, the gene-editing construct had been distributed to a broad range of tissues, including the bone

marrow, lymph nodes, and spleen, and had reached CD4+ T cells, and that the SIV genome was effectively cleaved from infected cells.

The new study is a continuation of efforts by Dr. Khalili, Dr. Burdo, and colleagues to develop a novel gene-editing system using CRISPR-Cas9 technology – the subject of the 2020 Nobel Prize in Chemistry – to specifically remove HIV DNA from genomes harboring the virus. The researchers have shown previously that their system can effectively eliminate HIV DNA from cells and tissues in HIV-infected small animal models, including HIV-1 humanized mice.

“This work is a critical step to initiating human clinical studies for a cure to HIV,” stated Daniel Dornbusch, CEO of Excision. “Researchers have searched for a cure for viruses such as HIV for decades. This important work brings us a step closer to evaluating the safety and efficacy of a single infusion to cure infected people around the world. We are proud of the team’s diligent work and effort and look forward to progressing this important product to human clinical trials.”

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Editor’s Note: Kamel Khalili is Co-Founder and Chief Scientific Consultant, and holds equity in Excision BioTherapeutics, which has licensed the viral gene editing technology from Temple University. Kamel Khalili and Rafal Kaminski are named inventors on patents that cover the viral gene editing technology. Tricia Burdo and Jennifer Gordon hold equity in Excision BioTherapeutics. These named researchers are employed by Temple University, and conduct research activities sponsored by the company. Questions regarding their affiliations with Temple University may be directed to **coisom@temple.edu.**

In addition to owning the viral gene editing technology that Excision is licensing, Temple University also holds an equity interest in Excision. As a result of these interests, Temple University could ultimately potentially benefit financially from the outcome of this research. These interests have been reviewed and approved by Temple University in accordance with its Institutional Conflict of Interest policy. Questions about this can be directed to **coitemple@temple.edu.**

About Excision BioTherapeutics Inc.

Excision BioTherapeutics develops CRISPR-based therapeutics to cure viral infectious diseases. Excision is the first company in history to remove viral genomes from animals and achieve functional cures in HIV with a therapeutic. The company’s pipeline includes potential cures for JC virus/PML, Hepatitis B, Herpes Simplex Virus, and SARS-CoV-2. The foundational technology was developed at Kamel Khalili's lab at Temple University and Jennifer Doudna’s lab at UC Berkeley. Excision is located in San Francisco, CA and is supported by **Artis Ventures**, **Norwest Venture Partners**, **Abstract Ventures**, **SilverRidge Capital Partners**, and **Gaingels**. The company is preparing to submit its first IND for EBT-101, its lead program in HIV in 2020. For more information visit **www.excision.bio**.

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