

Researchers propose ambitious new strategies for AIDS vaccine research

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Researchers at the Yerkes National Primate Research Center, Emory University, believe conventional vaccine strategies should not be the only avenue explored in the development of an effective AIDS vaccine. Based on studying simian immunodeficiency viruses (SIVs) in African nonhuman primates, they propose an additional new approach to the AIDS vaccine research agenda in a commentary featured in the August issue of *Nature Medicine*. Their recommendations outline specific research priorities and describe how each may lead to a novel "out of the box" approach for developing an AIDS vaccine.

"Developing an effective <u>AIDS</u> vaccine has eluded scientists because the virus is tricky," says Guido Silvestri, MD, a Yerkes affiliate scientist and director of clinical virology at the University of Pennsylvania School of Medicine and lead author of the commentary. Silvestri, along with coauthor James Else, DVM, associate director for veterinary resources at Yerkes, writes, "Over 25 years after the discovery of HIV as the etiological agent of AIDS, no effective vaccine for the disease is available."

Most vaccines are based on conventional strategies that work by triggering the body's immune system to produce antibodies or killer T cells against the invading organism. The AIDS virus, however, attacks the immune system, leaving it handicapped and unable to mount an immune response. Therefore, conventionally designed AIDS vaccines that have been clinically assessed to date have failed to protect vaccinated individuals from HIV transmission or disease progression.



This has been demonstrated in two large-scale clinical trials aimed, respectively, at eliciting HIV specific-antibodies to neutralize the virus and stimulating the immune system's "killer T-cells" to target the virus.

"To put it another way, a conventional vaccine strategy can be compared to using military might to destroy an enemy (in this case, the virus). A less conventional strategy could be to persuade the enemy not to attack you anymore," Silvestri explains. Alternative strategies may include development of AIDS vaccines that make infected individuals resistant to disease progression or resistant to the virus by reducing the number of cells the virus can infect.

Silvestri and Else propose that lessons learned from studying SIVs in their natural nonhuman primate hosts may provide a path to an effective AIDS vaccine. SIVs are found exclusively in African nonhuman primate species and represent the original source of human immunodeficiency viruses (HIV-1 and HIV-2). More than 40 species of African monkeys are infected in the wild with SIVs. Yet, virtually none with the exception of chimpanzees progresses to HIV/AIDS or gets sick. Evolution has enabled them to adapt to SIVs and co-exist peacefully with chronic infection.

"Nature is giving us a message," says Silvestri. "Figure out how these monkeys can deal with the virus, and then maybe you can get humans to do the same thing." In particular, Silvestri notes additional studies of sooty managbeys - a medium-sized African monkey - are critical for the AIDS vaccine effort and understanding why SIV infection does not progress to HIV/AIDS. SIV-infected sooty mangabeys develop a high viral load that does not increase their risk for developing AIDS. Additionally, the SIV virus is rarely transmitted from mothers to babies.

Silvestri also notes that with its large colonies of uninfected and naturally infected sooty mangabeys, "Yerkes has a unique resource for <u>AIDS</u>



<u>vaccine</u> research and every effort needs to be made to preserve and expand this colony of animals."

For nearly eight decades, the Yerkes National Primate Research Center, Emory University, has been dedicated to conducting essential basic science and translational research to advance scientific understanding and to improve the health and well-being of humans and nonhuman primates. Today, the center, as one of only eight National-Institutes of Health-funded national primate research centers, provides leadership, training and resources to foster scientific creativity, collaboration and discoveries. Yerkes-based research is grounded in scientific integrity, expert knowledge, respect for colleagues, and open exchange of ideas and compassionate quality animal care.

Within the fields of microbiology, immunology, neuroscience and psychobiology, the center's research programs are seeking ways to: develop vaccines for infectious and noninfectious diseases, such as AIDS and Alzheimer's disease; treat cocaine addiction; interpret brain activity through imaging; increase understanding of progressive illnesses such as Parkinson's and Alzheimer's; unlock the secrets of memory; determine behavioral effects of hormone replacement therapy; address vision disorders; and advance knowledge about the evolutionary links between biology and behavior.

Source: Emory University (<u>news</u>: <u>web</u>)

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