Targeting HIV: Moving closer to a potential cure

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**Tri-specific antibody targets and neutralizes 99.5% of HIV-1 virus strains**

A team of researchers at IBBR, led by Dr. Yuxing Li, Associate Professor at the University of Maryland School of Medicine, Baltimore, and Principal Investigator at the Institute for Bioscience and Biotechnology Research (IBBR), Rockville, is showing how engineered multi-specific antibodies appear to be highly effective at preventing infection across a broad range of HIV-1 virus strains.

Over 36 million people worldwide are currently infected with HIV and the disease has claimed another 35 million lives since the start of the epidemic (www.hiv.gov). Effective treatment of HIV infection currently involves using combinations of antiretroviral drugs (ARV). While ARV treatment can improve the overall quality of life of HIV-positive individuals, better alternative treatments are needed since they can cause undesirable side effects and patients can become resistant to ARV therapy.

Immunotherapeutics, molecules derived from the immune system, can be used to specifically target and neutralize HIV-1 virus particles. Several of these broadly neutralizing antibodies (bNAbs) are being developed and preliminary trials indicate that these individual bNAbs are safe, well-tolerated, and can reduce HIV-1 infection early on. However, treatment is not associated with long-term reductions in virus levels and, due to HIV's ability to rapidly mutate, resistant strains can emerge. Additionally, the risk of transmission still exists.

Dr. Li’s laboratory successfully created a bispecific antibody (bi-NAb) combining two bNAbs and tested it on a panel of 208 strains of HIV virus that are prevalent in humans. “The bi-NAb neutralized 95% of the circulating HIV-1 viruses, which is superior to any single agent,” said Dr. Li. “We further improved antiviral potency by engineering a tri-NAb and found that it can inhibit 99.5% of circulating HIV-1 viruses.” This technology could lead to development of the broadest-spectrum anti-HIV-1 immunotherapeutic and preventive treatment that exist worldwide.

This research, published in *Nature Communications*, February 28, 2018, included contributions from scientists at
IBBR, National Institutes of Allergy and Infectious Diseases, The Scripps Research Institute, and International AIDS Vaccine Initiative. In addition to Dr. Li, authors of this study were James Steinhardt, Chi-I Chiang, Lin Lei, Andrey Galkin, and Alexander Andrianov from IBBR, Javier Guenaga from International AIDS Vaccine Initiative, Hannah Turner and Andrew Ward from The Scripps Research Institute, Krisha McKee, Mark Louder, Sijy O'Dell, Nicole Doria-Rose, Robert Bailer, and John Mascola from Vaccine Research Center at National Institutes of Allergy and Infectious Diseases.

"At IBBR, we strive to develop solutions to major health challenges that enhance quality of life through science and discovery," said Dr. Thomas Fuerst, IBBR Director. “Dr. Li’s work has the potential to eliminate hidden HIV-1 reservoirs in patients, prevent transmission of the disease, and offer the hope of a cure from HIV infection to millions of people around the world.”

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