



MEDICAL EDUCATION AND RESEARCH GRANT OUTCOME REPORT

Reconstructing HIV Sequence Histories to Identify Potent Immune Responses

On the road to stopping HIV replication

By understanding how HIV avoids initial immune responses, researchers believe they may be able to chart a path toward a vaccine

► **Description:** HIV remains a major public health problem, but researchers have discovered that prophylactic drug or microbicide use may prevent infection following exposure. Some believe there is a potent natural immune response against HIV that occurs early after infection, but is overwhelmed as the virus replicates and mutates. Better understanding of this process will be a major component of an HIV vaccine.

► **Results:** The investigators developed a method using a rhesus macaque model and SIV (the virus that causes simian HIV) to identify early immune responses to SIV from which the virus rapidly escapes. Identification of these early immune responses would allow the design of a vaccine that would build upon these potent responses to improve the function of a HIV vaccine. The

A novel single cDNA amplicon pyrosequencing method for high-throughput, cost-effective sequence-based HLA class I genotyping

Simon M. Lank^a, Roger W. Wiseman^a, Dawn M. Dudley^b, David H. O'Connor^{a,b,*}

^a Wisconsin National Primate Research Center, University of Wisconsin-Madison, Madison, Wisconsin, USA

^b Department of Pathology and Laboratory Medicine, University of Wisconsin-Madison, Madison, Wisconsin, USA

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ABSTRACT

Human leukocyte antigen (HLA) genotype influences the immune response to pathogens and trans tissues; accurate HLA genotyping is critical for clinical and research applications. Sequence-based HLA genotyping is limited by the cost of Sanger sequencing genomic DNA (gDNA) and resolving cis/trans amplicons. We present an assay for sequence-based HLA genotyping by titanium reduction of PCR products. The amplicon is predicted to unambiguously resolve 85% of known alleles. A panel of 48 previously typed samples was assayed with this method, demonstrating 100% non-null allele typing concordance. This technique can multiplex at least 768 patients per sequencing run with multiplexed

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investigators were unable to translate this method from the SIV model to the HIV model using human samples during the course of this grant. However, the work on the genetic material of the virus did result in significant advances that may aid future HIV vaccine studies.

► **Timeline for Application of Results:** 5 to 7 years

► **Next Steps:** The investigators are seeking grant funding to study SIV-specific immune responses in the intestinal mucosa. This would allow them to use the techniques developed during this grant to sequence the SIV genome and help identify the immune responses necessary to include as part of a future HIV vaccine for humans.

GRANT FACTS

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