
Monoclonal Antibody-based methodologies for the detection and quantification of the HIV-1 accessory protein VPR in biological samples

Description of Technology:

This invention provides both the monoclonal antibodies to HIV-1 viral protein R (Vpr) and the hybridoma cell lines that provide monoclonal antibodies to HIV-1 Vpr. Methods for the use of such antibodies in the detection of HIV-1 infection are also provided.

There is no cure for acquired immune deficiency syndrome (AIDs) which results from human immunodeficiency virus (HIV)-1. Therefore, methods to determine HIV-1 infection levels remain the best defense in the fight against AIDS and HIV. Currently, the progression of HIV-1 is monitored by measuring the number of CD4 lymphocytes and the quantity of viral RNA in the blood. During HIV-1 infection, accessory HIV-1 proteins, such as viral protein R (Vpr), are also produced. Vpr may enter cells via non-receptor mechanisms to influence cellular regulatory mechanisms or to facilitate viral replication. Because Vpr is produced on HIV-1 infection, it may be a suitable target for the detection of HIV-1 at all stages of HIV-1 infection as well as those changes that lead to the complications associated with HIV.

This invention provides monoclonal antibodies against HIV-1 viral protein R (Vpr), the respective hybridoma cell lines expressing the protein, and a means for detecting HIV-1 Vpr. The hybridoma cell line is selected from a group of hybridoma cell lines 9F12 and 10F2. The monoclonal antibody (chimeric, humanized or label conjugated) competitively inhibits binding of a second hybridoma produced antibody against HIV-1 Vpr. The antibody-antigen complex that forms can be detected in the serum, plasma or urine and quantified. The primary antibody is detectably labeled, enabling the complex to be detected.

The patent application directed to this invention also claims methods for detection, including immunoassays (ELISA) and immunoaffinity-capillary electrophoresis. The amount of detected HIV-1 Vpr is compared to a standardized control sample for determining the progress HIV infection

Applications:

Regulatory and accessory proteins such as Vpr circulate at detectable levels in the blood and are likely derived from degraded virions or released from infected cells. Vpr has been proposed to correlate with one or more complications of HIV-1 infection. This technology, which enables Vpr to be detected, may be useful in assays for monitoring the progress of complications associated with HIV-1 infections including neuropathy and metabolic syndrome, which includes elevation of triglycerides and cholesterol and resistance to insulin, which can cause diabetes and inappropriate body fat distribution.



Advantages

Previously there has been no clinical assay to measure the level of HIV-1 regulatory or accessory proteins in biological fluids. In so far as Vpr is produced on HIV-1 infection and may correlate with one or more of the complications of HIV-1 infections, the measurement of Vpr may be important in the diagnosis and management of these complications.

Development Status:

- Monoclonal antibodies against HIV-1 viral protein R (Vpr) have been produced
- Hybridoma cell lines expressing the monoclonal antibodies have been created
- Use of these antibodies to detect HIV-1 Vpr has been demonstrated
- These materials are available for diagnostic and therapeutic development

Inventors:

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Publications:

Effects of transgenic expression of HIV-1 protein Vpr on energy metabolism in mice Am J Physiol Endocrinol Metab. 2007 Jan;292(1):E40-8. Epub 2006 Aug 1. [[Pubmed reference](#)]

Patent Status:

DHHS Reference No. E-141-2003, PCT Application Serial No. PCT/US2005/022135

Licensing Status:

Available for exclusive or nonexclusive licensing

Licensing Contact:

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Collaborative Research Opportunity:

The National Institute of Diabetes and Digestive and Kidney Diseases, Kidney Diseases Branch is seeking parties interested in collaborative research to further characterize cellular mechanisms behind Vpr release and to study the effect of Vpr on tissue functions and the levels of Vpr in patients with metabolic syndrome. Please contact Jeffrey B. Kopp (NIDDK) at jbkopp@nih.gov or Rochelle S. Blaustein at Rochelle.Blaustein@nih.gov for more information.



Research Focus and Selected Publications for Principal Investigator

Jeffrey B. Kopp, M.D., Kidney Disease Branch

Work in Dr. Kopp's laboratory focuses on the study of focal segmental glomerulosclerosis (FSGS). FSGS occurs in several forms, including idiopathic FSGS, FSGS in association with HIV-1 infection, and FSGS occurring as a consequence of glomerular hyperfiltration due to reduced renal mass. FSGS is characterized by accumulation of glomerular extracellular matrix protein (fibrosis), with progressive loss of kidney function.

His laboratory has sought to identify the HIV-1 genes responsible for FSGS, using a series of transgenic mice which bear either subgenomic viral genomes or single viral genes. He has recently developed a mouse that expresses Vpr in podocytes in an inducible fashion, resulting in proteinuria and FSGS and are pursuing the mechanisms by which Vpr induces FSGS. In addition, because it has been determined that HIV-1 Vpr is expressed at low levels in adipose tissues and can a) circulate in the blood, b) regulate lipid and fatty acid metabolism and c) alter fuel selection for oxidation in fasted state, effect of VPR on human glomeruli and in cultured podocytes is also being studied.

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3. Zhang Y, Choyke PL, Lu H, Takahashi H, Mannon RB, Zhang X, Marcos H, Li KC, Kopp JB Detection and localization of proteinuria by dynamic contrast-enhanced magnetic resonance imaging using MS325. *J Am Soc Nephrol* (16): 1752-7, 2005. [[Full Text/Abstract](#)]
4. Zaragoza C, Li RM, Fahle GA, Fischer SH, Raffeld M, Lewis AM Jr, Kopp JB Squirrel monkeys support replication of BK virus more efficiently than simian virus 40: an animal model for human BK virus infection. *J Virol* (79): 1320-6, 2005. [[Full Text/Abstract](#)]
5. Orloff MS, Iyengar SK, Winkler CA, Goddard KA, Dart RA, Ahuja TS, Mokrzycki M, Briggs WA, Korbet SM, Kimmel PL, Simon EE, Trachtman H, Vlahov D, Michel DM, Berns JS, Smith MC, Schelling JR, Sedor JR, Kopp JB Variants in the Wilms' tumor gene are associated with focal segmental glomerulosclerosis in the African American population. *Physiol Genomics* (21): 212-21, 2005. [[Full Text/Abstract](#)]
6. Dickie P Roberts A Uwiera R Witmer J Sharma K Kopp JB Focal glomerulosclerosis in proviral and c-fms transgenic mice links Vpr expression to HIV-associated nephropathy. *Virology* (322): 69-81, 2004. [[Full Text/Abstract](#)]

