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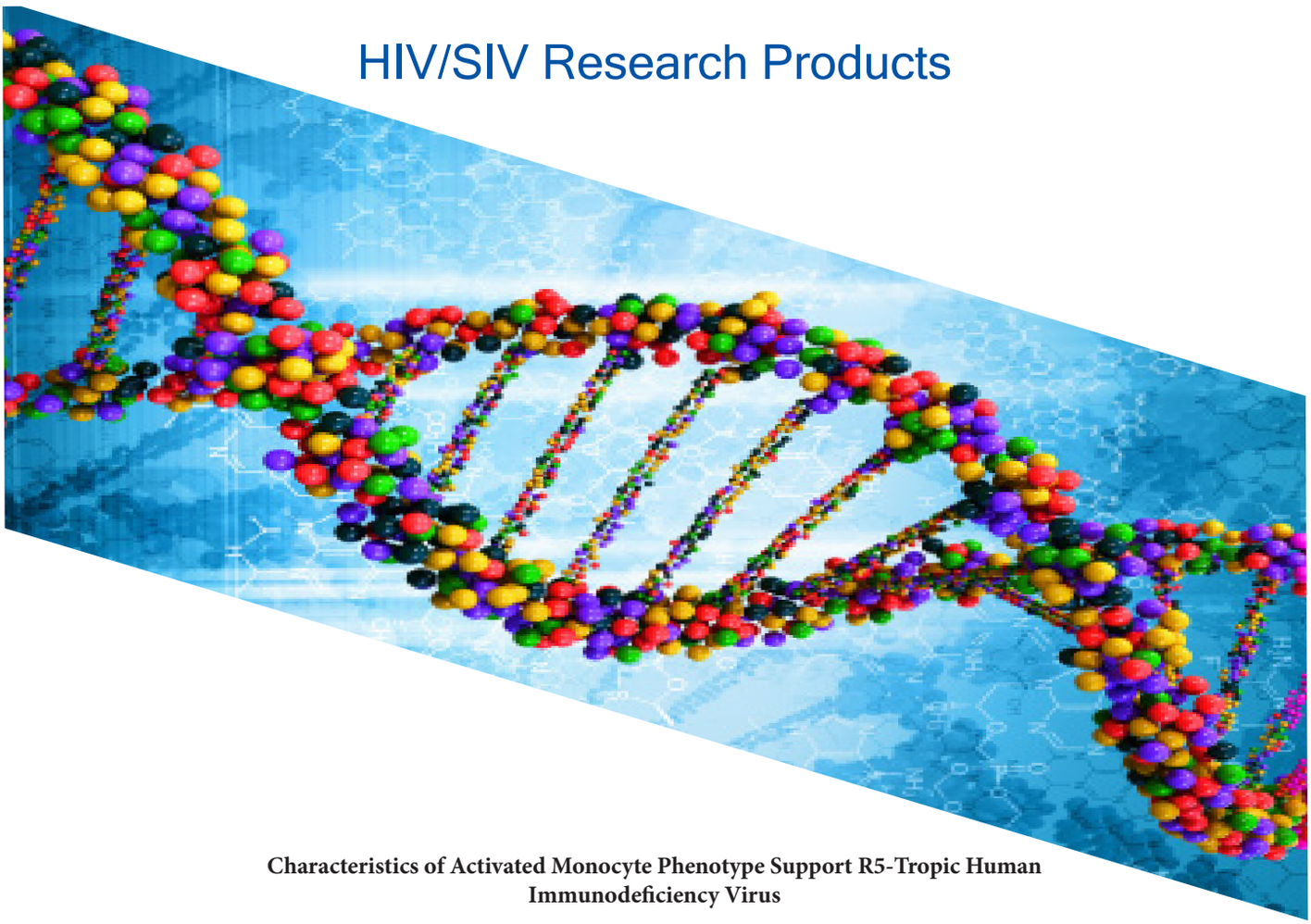
Life Science Products

# HIV/SIV Research Products



**Characteristics of Activated Monocyte Phenotype Support R5-Tropic Human Immunodeficiency Virus**


ABSTRACT

Background: Microbial translocation has been recognized as an important factor in monocyte activation and contributing to AIDS pathogenesis with elevated plasma lipopolysaccharide (LPS) levels, as a marker for microbial translocation, seen in advanced HIV disease. Therefore, the current study was undertaken to assess monocyte activation in vitro by LPS and to determine its impact on monocyte phenotype. Methods: Monocytes from non-HIV-infected donors were analyzed for CD14, CD16, CD69, TNF, and CCR5 by flow cytometry pre- and poststimulation with LPS. In-vitro cultures were then set up to expose non-activated and activated monocytes to R5-, X4-, and dual (R5/X4)-tropic viruses; and the amount of HIV present on the cells was assayed. Results: Non-HIV-infected monocytes, after LPS stimulation, were confirmed to have an activated phenotype with increase in CD16 and CD69 surface expressions ($p<0.05$). The activation phenotype was supported by increase in TNF production, $p<0.05$. The activated monocytes had increased surface CCR5 (from 21% to 98%; $p=0.05$); and were found to have more R5-tropic virus than non-activated monocytes ($p<0.05$). Conclusions: Following activation by LPS, non-HIV-infected monocytes were found to have increase in surface CCR5. These activated monocytes, when exposed to R5-tropic virus, were found to have more virus compared to non-activated monocytes. The significance of the findings could lie in explaining how microbial translocation plays a role in HIV progression; and possibly promoting CCR5-directed strategies in treating HIV.



Munsaka, Sody M., Melissa Agsalda, David Troelstrup, Ningje Hu, and Yu and Bruce Shiramizu. "Characteristics of Activated Monocyte Phenotype Support R5-Tropic Human Immunodeficiency Virus." Immunology and Immunogenetics Insights. Libertas Academica, 10 Mar. 2009. Web. 07 June 2012. <http://www.la-press.com/characteristics-of-activated-monocyte-phenotype-support-r5-tropic-huma-article-a1348>.

## HIV/SIV Research Products

| Reference | Product Description | Pack Size |
|---|---|---|
| XB-1000 | HIV-1 p24 ELISA Kit | 96 Tests |
| XB-1005 | HIV-1 p24 Immune Complex Dissociation Kit | 96 Samples |
| XC-1000 | HCV Core Antigen ELISA Assay | 96 Wells |
| XC-1005 | HCV Core Antigen Immune Complex Dissociation Kit | 96 Wells |
| SK845 | SIV p27 Assay | 96 Tests |
| EZ-1700 | Integrase Assay Kit (Wild-Type) | 96 Wells |
| EZ-1800 | Integrase Assay Kit (Mutant, N155H) | 96 Wells |
| INT832 | HIV-1 Integrase Enzyme (Wild-Type) | 100ug |
| INT833 | HIV-1 Integrase Enzyme (Mutant, N155H) | 100ug |
| AB-INT100 | HIV-1 Integrase Antibody (Rabbit, Polyclonal) | 100ug |

**Identification of novel host-oriented targets for Human Immunodeficiency Virus type 1 using Random Homozygous Gene Perturbation**

Abstract

Background: Human Immunodeficiency Virus (HIV) is a global threat to public health. Current therapies that directly target the virus often are rendered ineffective due to the emergence of drugresistant viral variants. An emerging concept to combat drug resistance is the idea of targeting host mechanisms that are essential for the propagation of the virus, but have a minimal cellular effect.

Results: Herein, using Random Homozygous Gene Perturbation (RHGP), we have identified cellular targets that allow human MT4 cells to survive otherwise lethal infection by a wild type HIV-1NL4-3. These gene targets were validated by the reversibility of the RHGP technology, which confirmed that the RHGP itself was responsible for the resistance to HIV-1 infection. We further confirmed by siRNA knockdowns that the RHGP-identified cellular pathways are responsible for resistance to infection by either CXCR4 or CCR5 tropic HIV-1 variants. We also demonstrated that cell clones with these gene targets disrupted by RHGP were not permissible to the replication of a drug resistant HIV-1 mutant.

Conclusion: These studies demonstrate the power of RHGP to identify novel host targets that are essential for the viral life cycle but which can be safely perturbed without overt cytotoxicity. These findings suggest opportunities for the future development of host-oriented therapeutics with the broad spectrum potential for safe and effective inhibition of HIV infection.

Mao, Hanwen, Hanson Chen, Zena Fesseha, Shaojing Chang, Huong Ung-Medoff, Jassica Van Dyke, Manu Kohli, Wu-Bo Li, Michael Goldblatt, and Michael S. Kinch. "Identification of Novel Host-oriented Targets for Human Immunodeficiency Virus Type 1 Using Random Homozygous Gene Perturbation." Virology Journal. 29 Sept. 2009. Web. 07 June 2012. <http://www.virologyj.com/content/6/1/154>.

**Restricted HIV-1 replication in placental macrophages is caused by inefficient viral transcription**

ABSTRACT

HIV-infected PM show restricted replication as compared with MDM. We aimed to determine at what point in the viral replication cycle this restriction occurs in PM as compared with MDM. We performed Alu-LTR PCR for proviral DNA to detect differences in HIV integration, realtime RT-PCR to measure env and gag mRNA levels, and Western blot analysis to detect differences in viral protein expression. PM and MDM were infected with HIV-1 BaL, and DNA was extracted after 24 h and at 6 days p.i. for real-time PCR studies. At 6 and 12 days p.i., cells were lysed for Western blot analyses. We found no difference in viral integration between PM and MDM but significantly lower levels of viral protein gp120 in PM than in MDM. Real-time RTPCR analyses revealed 24-fold less env mRNA and tenfold less gag mRNA in PM. These results suggest that HIV-1 restriction in PM occurs at the level of transcription. This study is significant, as it advances our understanding of HIV-1 infection in PM and its contribution to decreased in utero vertical transmission.

Garcia-Crespo, K., C. Cadilla, R. Sholasky, and R. L. Melendez. "Restricted HIV-1 Replication in Placental Macrophages Is Caused by Inefficient Viral Transcription." Journal of Leukocyte Biology. Journal of Leukocyte Biology, 7 Dec. 2009. Web. 07 June 2012. <http://www.jleukbio.org/content/87/4/633.full>.

**Heterosubtypic Protection against Pathogenic Human and Avian Influenza Viruses via In Vivo Electroporation of Synthetic Consensus DNA Antigens**

Abstract

Background: The persistent evolution of highly pathogenic avian influenza (HPAI) highlights the need for novel vaccination techniques that can quickly and effectively respond to emerging viral threats. We evaluated the use of optimized consensus influenza antigens to provide broad protection against divergent strains of H5N1 influenza in three animal models of mice, ferrets, and non-human primates. We also evaluated the use of in vivo electroporation to deliver these vaccines to overcome the immunogenicity barrier encountered in larger animal models of vaccination.

Methods and Findings: Mice, ferrets and non-human primates were immunized with consensus plasmids expressing H5 hemagglutinin (pH5HA), N1 neuraminidase (pN1NA), and nucleoprotein antigen (pNP). Dramatic IFN-c-based cellular immune responses to both H5 and NP, largely dependent upon CD8+ T cells were seen in mice. Hemaggutination inhibition titers classically associated with protection (.1:40) were seen in all species. Responses in both ferrets and macaques demonstrate the ability of synthetic consensus antigens to induce antibodies capable of inhibiting divergent strains of the H5N1 subtype, and studies in the mouse and ferret demonstrate the ability of synthetic consensus vaccines to induce protection even in the absence of such neutralizing antibodies. After challenge, protection from morbidity and mortality was seen in mice and ferrets, with significant reductions in viral shedding and disease progression seen in vaccinated animals.

Conclusions: By combining several consensus influenza antigens with in vivo electroporation, we demonstrate that these antigens induce both protective cellular and humoral immune responses in mice, ferrets and non-human primates. We also demonstrate the ability of these antigens to protect from both morbidity and mortality in a ferret model of HPAI, in both the presence and absence of neutralizing antibody, which will be critical in responding to the antigenic drift that will likely occur before these viruses cross the species barrier to humans.

Laddy, Dominick J., Jian Yan, Michele Kutzler, Darwyn Kobasa, Gary P. Kobinger, Amir S. Khan, Jack Greenhouse, Niranjan Y. Sardesai, Ruxandra Draghia-Akli, and David B. Weiner. "Heterosubtypic Protection against Pathogenic Human and Avian Influenza Viruses via In Vivo Electroporation of Synthetic Consensus DNA Antigens." Plos One. 25 June 2008. Web. 7 June 2012. <www.plosone.org>.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