Novel, Immunogenic Epitopes for use in an HIV Vaccine

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BACKGROUND

The Human Immunodeficiency Virus (HIV) has evolved a number of mechanisms of evading the human immune system. One way is through a high level of mutation, which makes it difficult to develop a vaccine that stimulates protective immunity against all of the different HIV variants. Therefore, scientists are searching for a general surrogate maker that could be used to target any HIV-infected cell regardless of its mutational status.

In this regard, scientists have recently focused their attention on so-called cryptic peptides of HIV. Cryptic peptides are non-functional HIV proteins that are produced due to translational errors that occur in HIV-infected cells. Because these cryptic peptides are commonly produced and then presented on the surface of the HIV-infected cells, it is thought they may be good surrogate markers and targets for any HIV-infected cell.

TECHNOLOGY DESCRIPTION

Investigators at UCSF, St. Mary's College, University of Wisconsin and University of Sao Paulo identified 199 unique, HIV cryptic peptides. A study in HIV-positive acute (n=28) and chronically infected (n=21) patients undergoing treatment with multiple anti-retrovirals showed that a number of the cryptic peptides were able to elicit an immune response from the patient's peripheral blood mononuclear cells. In both acute and chronic cohorts the response to the cryptic peptides was stronger and broader after treatment with anti-retrovirals and was stronger and broader in chronic patients compared to acute patients. These results indicate that the anti-retrovirals exert mutational pressure on HIV, which increases with the duration of the infection. Interestingly, the cryptic peptides elicited an immune response even in patients who were not able to generate a T-cell response to functional viral proteins, suggesting that cryptic peptides are produced from cells containing latent or inactive virus.

Based on these results, the cryptic peptides could be very useful in the development of a vaccine because they may be able to control HIV replication by increasing the diversity and breadth of anti-HIV immunity. In addition, the fact that the cryptic peptides are produced in cells containing latent virus presents a unique opportunity to specifically target latently infected cells, which would enhance virus eradication strategies.

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OTHER INFORMATION

KEYWORDS

HIV, Peptides

CATEGORIZED AS

- Medical
  - Diagnostics
  - Disease: Autoimmune and Inflammation
  - Research Tools
  - Screening
  - Therapeutics
  - Vaccines
- Research Tools
  - Screening Assays

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Future work will include: (1) identifying clinical correlations between T-cell responses against cryptic peptides and HIV-1 viral load and HIV-1 in the latent reservoir; and (2) cloning cryptic peptide-specific T-cells and measuring their ability to recognize and kill HIV-1 infected cells in vitro.

APPLICATIONS

- Preventative vaccine
- Immunotherapeutic
- Use in combination with other vaccines or immunotherapeutics (such as the APOBEC-based vaccine approach)
- Diagnostic tool to monitor HIV immunity through responses to cryptic peptides
- Surrogate marker to measure the effectiveness of an anti-retroviral drug regimen against a latent viral reservoir

ADVANTAGES

- Effective against latent viral reservoirs
- Effective in patients who do not exhibit an immune response to traditional viral proteins

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