

DNA Vaccines And HIV / AIDS

Ricardo Belmontes, James Ham, Ricardo Paz, Emily Scott-Solomon Advisors: Professors Jill Rulfs and Helen G. Vassallo

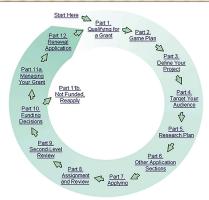
Great Problems Seminar: Heal The World

Problem Statement

HIV / AIDS affects over 33 million people worldwide, with the greatest number of victims located in developing countries. Conventional drugs only ease symptoms and do not cure the disease. A DNA vaccination that knocks down the CCR-5 gene could offer a solution to the disease.

Over 33 Million People Live with HIV/AIDS Worldwide

HIV is a retrovirus that infects T-cells which are central in adaptive immunity. It enters a cell by attaching to the CD4 receptor and the CXCR4 or CCR5 co-receptor. The HIV infection causes the body to lose cell immunity. The current treatment for HIV/AIDS, a triple cocktail which combines protease and reverse transcriptase inhibitors, costs about \$10,000-\$15,000 a year. However, the protease inhibitors increase the risk of cardiovascular disease and sudden heart failure in middle-aged HIV/AIDS patients.



Creating the Vaccine: Funding

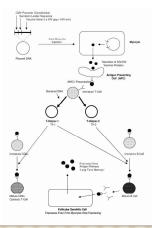
While the cost of delivering a DNA vaccine to a patient is cheap, the initial discovery cost of the vaccine is in the millions. In 2000, contemporary pharmaceutical companies estimated the cost of creating a new drug was \$403 million.

Two potential HIV / AIDS vaccine trials were scheduled, estimated to cost \$140 million and \$63 million dollars. In order to create a vaccine, additional funding would be needed from outside sources:

- •The Bill and Melinda Gates Foundation
- Private foundations
- Universities and research centers
- •National Institute for Health (NIH):
 - •Estimated budget in 2008 is \$2,905,219,000 with \$596.195.000 allocated for AIDS/HIV research.

DNA Vaccines

A DNA vaccine works by directly injecting DNA into the body, either the muscle or skin. Carrying the genetic information required, it begins producing antigens inside a host cell which will lead to a cellmediated immune response. The plasmid DNA vaccine carries the genetic code for a piece of pathogen antigen and transcribes it to the nucleus. The mRNA is translated into protein and then into peptides. The cytotoxic CD 8+ lymphocytes bind to the peptides and induce the cell-mediated immune response.



References:

- 1. Stevenson, Mario. "HIV-1 Pathogenesis." Nature Medicine 9 (2003): 853-60.
- 2. Dragic, Tatjana, Virginia Litwin, Graham P. Allaway, Scott R. Martin, Yaoxing Huang, Kirsten A. Nagashima, Charmagne Cavanan, Paul J. Maddon, Richard A. Koup, John P. Moore, and William A. Paxton. "HIV-1 entry into CD4 sup + cells is mediated by the chemokine receptor CC-CKR-5." Nature 381 (1996): 667-73.
- 3. Lehner, Thomas, Carl Doyle, Yufei Wang, Kaboutar Babaahmady, Trevor Whittall, Louisa Tao, Lesley Bergmeier, and Charles Kelly. "Immunogenicity of the Extracellular Domains of C-C Chemokine Receptor 5 and the In Vitro effects on Simian Immunodeficiency Virus or HIV Infectivity." The Journal of Immunology 166 (2001): 7446-455.
- 4. Bogers, Willy, Lesley A. Bergmeier, Julian Ma, Herman Oostmeijer, Yufei Wang, Charles G. Kelly, Peter Ten Haaft, Mahavir Singh, Jonathan L. Heeny, and Thomas Lehner. "A novel HIV-CCR5 receptor vaccine strategy in the control of mucosal SIV/HIV infection." AIDS 18 (2004): 25-36.
- 5. Chackerian, Bryce, Lindsey Briglio, Paul S. Albert, Douglas R. Lowy, and John T. Schiller. "Induction of Antibodies to CCR5 in Macaques and Subsequent Effects upon Challenge with an R5-Tropic Simian/Human Immunodeficiency Virus." Journal of Virology 78 (2004): 4037-047.
- 6. Yang, J., Y. W. Zhang, J. F. Huang, Y. P. Zhang, and C. Q. Liu. "Structure Analysis of CCR5 from Human and Primates," (2000).

Trial Areas: Lesotho and the United States

United States

- Developed nation
- Unstable economic and politics minimized
- •Focus can be made on effectiveness of vaccine Lesotho
- •270,000 people infected with AIDS (23.2% of population)
- •Relatively small area (11.720 sq miles)
- Presence of Riders for Health
- ·Variety of variables stereotypical of developing nations



Assessment:

Data

Name

• Determine if patients completed treatment and retuned for follow ups

Housing Location • Environmental factors that contribute to spread of

· Area in need of alternative distribution method

Blood Test

· Check HIV virus level

Results

Age

Dietary Habits Nutrition Level

Dates

Clinical Visitation • Followed inoculation regiments (grace periods between treatments)

· Determine most susceptible population to target

· Most treatment responsive age

Economic Status (Income)

Patient Health

· Check for gender specific side effects

· Determine most susceptible population to target · Determine price range affordable

Family History (if Available)

· Determine potential genetic diseases

· Other diseases that could be attributed to death if

History · Determine progression of HIV/AIDS in system

Allergies · Cease distribution to patient to avoid

hyperimmune response · Determine if certain medications heighten

> vaccination response · Determine if certain medications increase health

Prescriptions