AIDScience Vol. 1, No. 11, October 4, 2001

Urgency and optimism at the AIDS Vaccine 2001 conference

Marthali Nicodemus,[*1] Hakima Sbai,[2] and Anne S. De Groot[2]

[1]GAIA Vaccine Foundation, 365 Hope Street, Providence, Rhode Island 02906, United States
[2]TB/HIV Research Laboratory, Brown University, Providence, Rhode Island 02912, United States

[*]To whom correspondence should be addressed. E-mail: director@gaiavaccine.org

Introduction

Between 5 and 8 September 2001, researchers met in Philadelphia, Pennsylvania, at the AIDS Vaccine 2001 conference. The mood of the participants was cautious optimism: optimism about new approaches to HIV and AIDS vaccines and positive results in nonhuman primates. At the same time, around the world, 15,000 people each day were being infected with HIV.

Encouraging Progress

Margaret Johnston of the National Institute of Allergy and Infectious Diseases (NIAID) at the U.S. National Institutes of Health most eloquently expressed the optimism of conference attendees in a session entitled "The Preclinical Pipeline." Johnston said she has been encouraged by the establishment of several new organizations and funding mechanisms; the advances made in knowledge about the virus, vaccine technologies, and assay techniques; and the sheer number of candidate vaccines. She warned, however, that some aspects of HIV vaccine development, such as the clade issue, still need to be addressed.

Outlining efforts that are already underway, Johnston noted the proliferation of public and nonprofit efforts to speed and facilitate development of an HIV vaccine. These included France’s Agence Nationale de Recherches sur le SIDA, the European Union's EuroVac, the International AIDS Vaccine Initiative (IAVI), the South African AIDS Vaccine Initiative (SAAVI), the HIV Vaccine Initiative of the Joint United Nations Programme on HIV/AIDS (UNAIDS), and the United States’ Walter Reed Army Institute of Research, among others. She also listed the major advances that vaccine researchers have made in fundamental knowledge over the past few years: increased knowledge about the structure of the HIV envelope, a better understanding of how the virus enters target cells, and increased recognition of the important role T helper cells and cytotoxic T lymphocytes (CTLs) play in HIV and SIV infections. Concurrently, Johnston said, there have been advances in vaccine technologies such as codon-optimized DNA, novel nonreplicating viral vectors [adeno-associated virus (AAV), Sindbis, canarypox], bacterial vectors [Salmonella, Bacille Calmette-Guérin (BCG)], multi-epitope vaccines, engineered delivery vehicles, and inactivated-virus approaches. Methods to measure the efficacy of these new technologies have also advanced with the development of techniques like ELISPOT and tetramer binding assays, easier assays to measure neutralization, and the routine use of viral-load assays in primate-model studies.

All these advances have led to an increase in the number of research efforts underway to develop a vaccine against HIV/AIDS. One measure of progress is the number of vaccines entering phase I trials:

According to Johnston, up to 15 Investigational New Drug (IND) filings are anticipated in 2002, for instance. These INDs include novel protein and peptide approaches, new poxvirus vectors, novel DNA approaches, and other novel vectors (e.g., adenovirus, Sindbis, and Salmonella). She remained concerned, however, at the much smaller number of vaccines entering phase III trials, and she called for further increases in the preclinical pipeline to compensate for this decline.

Johnston also highlighted the number of non-clade B vaccines that are being researched all over the world, including the clade A modified vaccinia Ankara (MVA) and DNA vaccines that are currently in phase I trials in Kenya (Oxford University and IAVI), and the ALVAC (canarypox) and gp120 vaccines that are currently in phase II trials in Thailand (VaxGen/Aventis/U.S. Army). She cautioned, however, that the variability of HIV isolates needs to be investigated vigorously, and efforts need to concentrate on the potential for eliciting cross-clade responses. This, according to Johnston, will require researchers working with nonhuman primate models to measure cross-clade protection and correlate the data thus gathered with immunogenicity. She encouraged conference participants to start generating data describing cross-clade responses (*1*).

Working together

Participants emphasized both the success of existing collaborations and the importance of additional collaborations in HIV-vaccine research and in the testing of HIV vaccines. Although most vaccine research and development is taking place in the industrialized world, vaccine trials need to concentrate on sites in developing countries where HIV/AIDS is wreaking havoc. Funding organizations, researchers, and trial-site communities need to work together on a level heretofore unseen. One of the most striking collaborative efforts currently underway is the South African AIDS Initiative (SAAVI), which was outlined by Malegapuru Makgoba, an immunologist and president of the South African Medical Research Council (MRC), in a plenary session entitled "South Africa: A Case Study in Vaccine Implementation" (*2*).

Acknowledging that South Africa faces formidable obstacles in developing an HIV/AIDS vaccine, Makgoba stressed that there is an urgent need for a vaccine in that country, which has one of the highest HIV infection rates in the world (10% of the population was estimated to be HIV+ in 2000) . AIDS is at the top of the list of killers in South Africa in 2000: 40% of deaths last year of people aged 15 to 49 were attributed to the disease (*3*). Furthermore, most infected individuals there don't have access to HIV/AIDS therapeutics; thus, the development of an effective vaccine is all the more urgent. Unfortunately, candidate vaccines currently in trials may not be relevant to South Africa, said Makgoba, because South Africa needs an effective clade C vaccine.

Makgoba warned that the urgent need for an HIV vaccine should not lead to researchers from industrialized nations starting a "new scramble for Africa" and engaging in what he terms "scientific colonialism." He emphasized, however, that the compelling demand for HIV vaccines must be balanced with ethical imperatives that, ensure high-quality research and equitable power relationships between industrialized and developing nations. The challenges that must be met include creating equal partnerships in the leadership and direction of the research agenda.

SAAVI was developed to meet all these challenges, according to Makgoba. South Africa has ownership of the project so that "internationality" is related to national authority. The project is a coordinated approach based on the principles of "coherence and accountability to equity, funding, science and ethics"

(see box).

The South African AIDS Vaccine Initiative

"SAAVI's purpose is to galvanize South Africa's scientific community to address and focus on a national and regional health ... crisis," said Malegapuru Makgoba. The creators of the program were at great pains to ensure that SAAVI becomes a multi-disciplinary and trans-disciplinary effort, based on a system of a number of "teams", each focused on one aspect of the overall project. SAAVI's areas of concentration include developing a one or more vaccines; implementing vaccine trials; organizing advocacy and education programs; ensuring that ethical standards are adhered to and that human rights are protected; and developing human capital and infrastructure to implement all these aims.

SAAVI's ultimate goal is to make an affordable, effective, locally relevant vaccine within 10 years. Vaccine development projects already underway include research into a DNA and MVA vaccines. A DNA-gag candidate will be "ready to go soon", according to Makgoba. DNA-gag-env and MVA-gag vaccine candidates are expected to be ready for trials in 9 to 12 months.

Thus far, 250 local researchers have been recruited; R150 million (U.S. $18 million) in foreign funding has been secured; an international collaboration has been formed with 120 researchers at 10 institutions; R15 million (U.S. $1.8 million) has been invested in equipment and infrastructure; two vaccine trial sites have been established; and a central animal facility is being set up.

Although the project is fully underway, said Makgoba, SAAVI will need continuing support to achieve its goal. Ongoing intellectual partnerships are necessary, as well as manufacturing partners for Good Manufacturing Practice (GMP) and toxicity testing. More trial sites need to be established, and SAAVI will need access to vaccines that are in the pipeline elsewhere in the world.

Makgoba encouraged vaccine researchers to reach out to South Africa for collaborative studies, and emphasized the importance of including South African researchers as full partners in the vaccine effort. He reminded potential collaborators that they should leave "arrogance" at home (*2*).

During a session entitled "Global Challenges for Vaccine Implementation," José Esparza, coordinator of the UNAIDS HIV Vaccine Initiative, stressed efficacy as the most important aspect of a potential HIV vaccine. "Good science alone will not give us an HIV vaccine," he said. Because a vaccine is urgently needed, more clinical trials need to be conducted soon, and cross-clade reactivity needs to be investigated. "Multiple trials will have to be conducted simultaneously to assess the efficacy of different vaccine concepts and combinations against different HIV subtypes in different populations," said Esparza.

To speed clinical trials, Esparza advocated the World Health Organization (WHO) program of National AIDS Vaccine Plans in developing countries. These plans aim to give national authorities control of and responsibility for the trials taking place in their countries. In doing so, the WHO tries to "foster collaboration rather than competition," said Esparza. National AIDS Vaccine Plans have been adopted in Brazil, Thailand (where phase III trials are underway), Rwanda, and Uganda. In conclusion, Esparza stressed that successful vaccine trials and implementation programs must foster participation of the local community, address ethical issues that may arise, and provide access to future effective vaccines (*4*).

The note of optimism continued in other sessions describing collaborative phase III vaccine trials.

Donald Francis, of VaxGen, Inc., reported extremely high volunteer retention rates in the VaxGen AIDSVAX B/B phase III efficacy trials in North America and the Netherlands (*5*). Punnee Pitisutiithum provided additional evidence of effective recruiting and retention of volunteers in the course of the VAXGEN B/E trial in Thailand (*6*). Deborah Birx, of the Walter Reed Army Institute of Research in Rockville, Maryland, described the importance of HIV/AIDS vaccines to overseas military operations and emphasized the Army's particular interest in nonclade B and broadly cross-reactive (cross-clade) vaccines (*7*). Susan Buchbinder reported the extensive work of the U.S.-based Vaccine Trials Network (*8*).

From macaques to humans?

Much of the optimism at the conference was focused on the results of several animal studies currently underway. Harriet Robinson, of the Emory Vaccine Center and Yerkes Regional Primate Research Center in Atlanta, presented the results of a collaboration between the Emory Vaccine Center, Bernard Moss's laboratory at NIAID, and Janet McNicholl's laboratory at the U.S. Centers for Disease Control and Prevention (*9*). Seven months after immunizing rhesus macaques with a SHIV-89.6 Gag-Pol-Env or a Gag-Pol DNA vaccine at 0 weeks and 8 weeks and boosting with a SHIV-89.6 Gag-Pol-Env or Gag-Pol recombinant MVA at 24 weeks, the macaques were challenged with SHIV-89.6P. Although all the vaccinated and control animals were infected after challenge, animals vaccinated with the DNA construct were able to control infection. The animals receiving the Gag-Pol-Env DNA/MVA vaccine controlled infection best: 31 of 32 animals that received this vaccine sustained viral RNA at or below the level of detection for more than 8 months (*9*).

Robinson emphasized the need to include as many of the viral proteins as possible in an HIV vaccine construct, because better protection was observed when Env (a highly variable protein) was included along with Gag and Pol. These experiments did not address HIV variability, because the vaccine vector and challenge virus are closely related (SHIV-89.6 and SHIV-89.6p), and some researchers question whether SHIV is the correct challenge model (*10*).

In spite of the questions raised about SHIV, Merck Pharmaceutical is going forward with development of its SHIV-challenged candidate vaccine that uses a replication-incompetent adenovirus or a DNA/adjuvant prime with an adenovirus boost (*11*). Using DNA/adenovirus and DNA/MVA approaches, they found that the DNA/adeno boost gave the best results. Monkeys that had prior immunity to adenovirus were less responsive to the adenovirus-vectored vaccine, although Merck reported improvement if DNA was used as primer. Merck also reported a correlation between the magnitude of CTL responses and the degree of protection against challenge. It was not clear from their presentation, however, whether the magnitude of the CTL reponses (against pools of peptides) was related to the breadth of responses (against many CTL epitopes) or to the size (number of spot-forming cells) of the response to a single epitope. Merck Pharmaceutical's use of peptide pools derived from consensus sequences also made it difficult to interpret their claim that they were able to elicit cross-clade responses.

Norm Letvin of Harvard Medical School in Boston believes that the "take-home message" provided by nonhuman primate experiments is that "a vaccine that induces CTL responses in monkeys should be an effective vaccine in humans." He also noted that the best predictors of vaccine "success" in the nonhuman primate model appeared to be CTL response before challenge and CD4 reactivity

post-challenge. He provided support for these statements in a review of experiments carried out in nonhuman primates in his laboratory and in the laboratories of other researchers over the past few years. Monkeys vaccinated to elicit CTL response (with plasmid DNA, pox viruses and gene-deleted adenoviruses) and then challenged with SHIV (and SIV) have low virus loads and thus slower disease progression. Letvin believes this kind of immunity can also be elicited in humans, and thus could confer the same kind of protection against the disease (*12*).

New approaches versus the usual suspects

A host of candidate vaccines were presented during two 180-minute sessions and during some sessions at the end of the conference. A large number of vectors were proposed, including recombinant AAV (rAAV). These vectors lack any wild type genes and consist only of the genes of choice and required expression segments. Phillip Johnson presented data that indicate that rAAV stimulate immune responses against SIV challenge in macaques (*13*). Johnson described the presence of durable antibody responses to the vaccine for up to 2 years in macaques, and he believes this is due to antigenic persistence. (He could detect the presence of ß-gal, a marker gene, in macaques for up to 17 months in parallel experiments.) Perhaps more important, he demonstrated protection against a heterologous challenge virus (SIV sm E660). His group has proposed a prime-boost (DNA followed by AAV) approach and is moving forward with human trials of rAAV HIV vaccines.

Herpes simplex virus 1 and 2 (HSV1 and HSV2) were also proposed as vectors. A team from Harvard Medical School is working on a HSV2 recombinant that expresses SIV Env and Gag in vitro and induces immune responses in rhesus macaques (*14*). A three-way collaboration between the University of Rochester in New York state, the University of New York, and Oxford University presented data that helper-free HSV1 amplicon particles elicit cellular immune responses even in mice that have previously been infected with HSV1 and, therefore, had preexisting immunity (*15*).

Another vaccine candidate that is entering phase I trials is a replicon vector based on the Venezuelan equine encephalitis virus (VEE). Ande West of the University of North Carolina, Chapel Hill, showed that VEE replicon particles expressing genes of interest, including an HIV clade C Gag, have proven to be safe and immunogenic in animal models, including primates (*15*). Through an international collaborative effort supported by IAVI, this VEE-replicon vaccine expressing Gag from a South African HIV-1 clade C isolate is in Good Manufacturing Practice (GMP) production and is scheduled to begin phase I trials in early 2002 (*16*).

A recombinant rabies virus (RV) vector with a similar tropism to HIV-1 but no integration in the host cell genome was also explored. This glycoprotein-deficient RV vector expressing HIV-1 gp160 has been shown to be able to efficiently infect and replicate in human mononuclear peripheral blood cells and human macrophages, and specifically target cells expressing CD4 and HIV-1 coreceptor (*17*).

Novel envelope immunogens that aim to increase the exposure of conserved neutralizing B-cell epitopes by stabilizing the association between gp120 subunits and the gp120-gp41 interaction have also been developed. These vaccine candidates include the development of disulfide-stabilized HIV-1 envelope glycoproteins (*18*) and native HIV-1 envelope glycoproteins formulated in proteoliposomes (*19*, *20*).

The role of innate immunity was not neglected at the conference. Bruce Beutler of the Scripps Research Institute in La Jolla, California, reviewed the role of the toll-like receptor family as signal transducers

that stand at the interface between host and pathogen and act as direct sensors of microbial infection. HIV does not induce innate immunity and is highly transmissible. Somehow activating innate immunity, on top of inducing a specific immune response, could improve the immunogenicity of HIV vaccines (*21*)(21).

The cross-clade issue

The team at Maxygen is trying to develop a cross-clade vaccine with their DNA-shuffling technology, which Robert Whalen described as "genetic recombination in a test tube." This technology can be used to create novel surface-antigen sequences from which the sequences with the best immunogenicity are selected. Maxygen is applying this technique to an HIV vaccine based on Env. They succeeded in developing Env genes with better immunogenicity than the parent sequences in mice. Maxygen is proposing that the shuffling technique may result in novel Env structures that may induce cross-clade responses (*22*).

Mark Newman of Epimmune presented information on the multi-epitope approach to HIV-vaccine development (*23*). Epimmune is manufacturing a vaccine based on 21 epitopes for phase I trials. This vaccine contains epitopes restricted by the class I HLA A2, A3, B7 as well as supertype DR (class II) epitopes derived from Pag, Pol, and Env. These epitopes were derived from a fairly limited analysis of 64 HIV isolates, of which 50% are clade B. Newman presented an analysis of the epitopes that highlighted their "conservancy" (conservation) across clades. He also described improved immune responses in mice to vaccine that included spacers between the epitopes. Newman emphasized data showing that they were able to induce a broader immune response using the epitope-based approach, compared to vaccination with the whole gene. He said that this might be due to the efficient induction of CTL responses against subdominant epitopes in the epitope-based approach.

Kent Weinhold of Duke University presented a variety of methods to evaluate cross-clade responses following vaccination of volunteers with available HIV vaccines (*24*). He found good cross-clade reactivity in some vaccinated volunteers and no cross-reactivity in others. He felt this variability in response could be linked to the HLA of the volunteer and emphasized the importance of developing vaccines that could stimulate immune responses against a broad range of T-cell epitopes, restricted by many different HLA. He said that "a vaccine with the highest number of highly conserved (across clades) epitopes restricted by many different alleles would be the best immunogen" for an HIV vaccine.

Bette Korber of Los Alamos National Laboratory in New Mexico argued in favor of a revolutionary "consensus" approach to vaccine design (*25*). She suggested that vaccines be developed from consensus sequences, because the sequences of consensus isolates would be more similar to those of each of the subtypes (A, C, B) than vaccines composed from one subtype (clade A, for example) would be to another subtype (a clade B or C, for example). She also reviewed her discovery of epitope-rich regions in the HIV genome. Korber and her colleagues mapped epitopes against consensus B sequences and found that most epitopes cluster in conserved regions of the virus. Discussion following her presentation raised the two possible explanations: (1) the epitopes are clustering because the HLA motifs for the epitopes have similar anchors (such as has been observed for HLA A3, A11, and A68, which would all restrict the same peptide, but responses would be classified as separate epitopes), and/or (2) epitopes were not detected in the variable regions of the genome because researchers had not examined immune responses using peptides containing those variable sequences. Nonetheless, her presentation emphasized the importance of conserved epitopes in HIV-vaccine design.

The meaning of diversity

Perhaps Paul Sharp of the University of Nottingham, U.K., sounded the most somber note of the entire meeting in his discussion of HIV diversity (*26*). He contrasted HIV diversity (30% in the Env gene) with poliovirus (9%), measles virus (3%), and influenza virus (4%) and noted that HIV has the highest diversity of any of these human pathogens. Sharp discussed variability between clades saying that variability between the M, N, and O groups is estimated at 32% overall (50% for the env gene), and between subtypes within clades, where the variability between subtypes within M, for example, is estimated at 14% (higher for env, 30%).

Although we have developed vaccines against viruses with similar mutation rates to HIV-1 (influenza A, for instance), Sharp warned that it will not be as easy to develop a vaccine for HIV-1 because the population biology of HIV-1 is different from that of influenza A. The diversity of influenza A is basically stable from year to year; whereas, the diversity of HIV-1 continues to expand.

Therapeutic vaccines

The most passionate plea for development of an AIDS vaccine was delivered by Bruce Walker of the Partners AIDS Research Center and Infectious Disease Unit at Massachusetts General Hospital in Boston, who reviewed his work on strategic treatment interruption in one of the final sessions (*27*). Outlining the optimism about therapeutic vaccines, he said that we know vaccination with such vaccines can boost immune response after infection and the infection can be controlled, at least for a time. But he also listed many obstacles in the way of therapeutic vaccines. These included viral diversity and immune escape, lack of sufficient helper T cell response and possible HLA specificity complications.

To address these problems, Walker called for collaboration between researchers. "Twenty years into the HIV epidemic," he said, "there are still no comprehensive data on even a single patient regarding the breadth and specificity of the immune response to the person’s own virus." He said that this gap in our knowledge can only be bridged if researchers are willing to share data and resources. Highlighting the devastating extent of the epidemic around the world, Walker emphasized the need for safe, effective, broadly immunogenic vaccines for use in therapeutic vaccination.

Conclusion

Although there is much to be optimistic about in the search for an effective HIV/AIDS vaccine, many issues still need to be addressed, and attitudes need to change. "Clade B centrism" is abating, and it is hoped not just to make way for "single-clade centrism." To settle the clade issue, multiple trials need to be conducted simultaneously in many parts of the world, and data on cross-reactivity in humans and nonhuman primates need to be gathered. Many more trials sites must be established, and funding organizations, researchers, and local communities must work together on an equal footing to speed up the search for a HIV vaccine. Researchers also need to move as quickly as possible to human trials to swiftly identify promising candidate vaccines and progress to testing them for efficacy. Although the development of a prophylactic vaccine seems very far off, if not impossible, therapeutic vaccines can play an important role by enabling HIV+ individuals to control the spread of the disease and thus save countless lives.

References and notes

1. M.I. Johnston, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract S9. Available online.

2. N.L. Letvin, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract L9. Available online.

3. "It's 'official': AIDS is SA's leading killer." South African Press Association/Agence France Presse report, September 16, 2001. Available on line.

4. J. Esparza, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract S15. Available online.

5. D. P. Francis, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract S10. Available online.

6. P. Pitisuttithum, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract S11. Available online.

7. D. L. Birx, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract S13. Available online.

8. S. Buchbinder, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract S14. Available online.

9. H.L. Robinson, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract 44. Available online.

10. L. Garrett, "Skeptical about AIDS vaccine: Testing method questioned." Newsday, September 5, 2001. Available online. Some researchers not attending AIDS Vaccine 2001 raised concerns about translating the success in animal models into potential human benefit. Harvard Medical School's Ronald Desrosiers (director of the New England Regional Primate Research Center in Southborough, Massachusetts) was quite outspoken in his criticism, saying, "I fail to understand where this optimism is coming from. I find it totally astounding, to the point of it being irresponsible, in many cases. What are they thinking?" Desrosiers says SHIV is so different from the wild type, that it produces a different disease; therefore, the vaccines are not protecting against SIV disease. SHIV is so virulent that it can obliterate CD4s in 2 weeks. Researchers like Desrosiers question whether SHIV disease can be a model for human AIDS. Letvin argues that this virulence makes it perfect for speeding up trials.

    But Desrosiers insists that every potential vaccine challenged so far only with SHIV should be retested with an SIV challenge. "If you look back to the early days when people started doing the first monkey trials, one of the things we learned was that you could get any results you wanted ... if you used the right challenge strain," he said in Newsday.

11. D.R. Casimiro, et al., paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract 303. Available online.

12. N.L. Letvin, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract L9. Available online.

13. P.R. Johnson, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract 2. Available online.

14. W. Lucas et al., paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract 301. Available online.

15. P.K. Hocknell et al., paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract 302. Available online.

16. A. West et al., paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract 5. Available online.

17. E. Reap et al., paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract 175. Available online.

18. H.D. Foley et al., paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract 307. Available online.

19. J.P. Moore et al., paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract S2. Available online.

20. C. Grundner, T. Mirzabekov, J. Sodroski, R. Wyatt, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract S4. Available online.

21. C. Grundner, T. Mirzabekov, J. Sodroski, R. Wyatt, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract 306. Available online.

22. B. Beutler, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract L4. Available online.

23. L. Xu, W. Zhang, X. Du, D.R. Burton, P.W.H.I. Parren, R.G. Whalen, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract 6. Available online.

24. M. Newman, B. Livingston, D. McKinney, R. Chesnut, A. Sette, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract 305. Available online.

25. K. Weinhold, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract S7. Available online.

26. B. Korber, B. Gaschen, K. Yusim, B. Foley, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract S8. Available online.

27. P.M. Sharp, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract L11. Available online.

28. B. Walker, paper presented at the AIDS Vaccine 2001 conference, Philadelphia, Pennsylvania, United States, 5-8 September 2001, Abstract L10.

29. Abstracts, posters, lectures and slides from the AIDS Vaccine 2001 conference are available online at http://63.84.172.40/ or http://www.aidsvaccine2001.org.