A human immunodeficiency virus 1 (HIV-1) clade A vaccine in clinical trials: stimulation of HIV-specific T-cell responses by DNA and recombinant modified vaccinia virus Ankara (MVA) vaccines in humans

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The immunogenicities of candidate DNA- and modified vaccinia virus Ankara (MVA)-vectored human immunodeficiency virus (HIV) vaccines were evaluated on their own and in a prime–boost regimen in phase I clinical trials in healthy uninfected individuals in the United Kingdom. Given the current lack of approaches capable of inducing broad HIV-neutralizing antibodies, the pTHr.HIVA DNA and MVA.HIVA vaccines focus solely on the induction of cell-mediated immunity. The vaccines expressed a common immunogen, HIVA, which consists of consensus HIV-1 clade A Gag p24/p17 proteins fused to a string of clade A-derived epitopes recognized by cytotoxic T lymphocytes (CTLs). Volunteers’ fresh peripheral blood mononuclear cells were tested for HIV-specific responses in a validated gamma interferon enzyme-linked immunospot (ELISPOT) assay using four overlapping peptide pools across the Gag domain and three pools of known CTL epitopes present in all of the HIVA protein. Both the DNA and the MVA vaccines alone and in a DNA prime–MVA boost combination were safe and induced HIV-specific responses in 14 out of 18, seven out of eight and eight out of nine volunteers, respectively. These results are very encouraging and justify further vaccine development.

INTRODUCTION

Since the first report of acquired immunodeficiency syndrome (AIDS) in 1981 and its subsequent recognition as a novel disease, an estimated total of 60 million people have become infected with the human immunodeficiency virus (HIV), of whom some 22 million have died (UNAIDS, 2001). The most affected continent is Africa, where 60% of world infections take place. Twenty years after the discovery, HIV continues to spread particularly in developing countries in a largely uncontrolled manner. The most realistic hope for bringing this situation under control is development of a safe, effective, accessible, prophylactic HIV vaccine.

It is generally believed that an effective HIV vaccine may have to stimulate both neutralizing antibodies and cell-mediated immune responses and do so both systemically and at mucosal sites (McMichael & Hanke, 2003). While the instability and inaccessibility of potentially neutralizing epitopes on primary HIV isolates have hampered the development of envelope-based vaccines (Kwong et al., 1998, 2002; Wyatt et al., 1998), a few new potent technologies

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capable of inducing high levels of circulating virus-specific CD8+ cytotoxic T lymphocytes (CTLs) are emerging (Hanke, 2003).

CTLs recognize, through their T-cell receptor, short HIV-derived peptides (8–10 aa long) presented by a ‘self’ major histocompatibility complex molecules called HLA in humans. Recognition of these HLA–peptide complexes in the context of the right accessory signals stimulates naive and precursor memory CTLs to proliferate and express effector functions. These include lysis of HIV-infected cells, which limits the production of new HIV virions, and production of soluble cytokines and chemokines that can directly or indirectly contribute to the control of HIV replication. The advantage of CTLs over antibodies is that the recognized peptides can originate from both surface and inner HIV proteins. The disadvantage is that CTLs cannot prevent the first wave of cell-free HIV from infecting host cells, i.e. induce sterilizing immunity. However, once CTLs become stimulated by antigen-presenting cells, they produce soluble factors relatively quickly that can, at least in vitro, prevent HIV from entering cells (Zhang et al., 1996; Price et al., 1998; Wagner et al., 1998; Stranford et al., 1999). Thus, providing that an individual is exposed to a low HIV dose, CTLs can theoretically prevent HIV from spreading and establishing a generalized infection by eliminating HIV-infected cells early in infection. Alternatively, CTLs can keep the virus at levels so low that both transmission to other individuals and progression to AIDS are prevented. The net effect of these actions might be that CTLs increase the threshold for infection and therefore decrease the HIV transmission rate (Hanke, 2003). However, these predictions can be only proven or disproven by first developing methodology for induction of T-cell responses in humans followed by a controlled efficacy clinical trial.

HIV-1 is a highly variable virus, for which intra-subtype variation could be as high as 20% and inter-subtype diversification can reach 35% of the amino acid sequence (Thomson et al., 2002). Clade B is the most common in Europe and North America, clades A, C and D dominate in Africa, and C is now the most widespread clade. In Nairobi, clade A currently causes about 70% of HIV infections (Neilson et al., 1999). Although some reports have demonstrated that cross-clade CD8+ T-cell responses can be detected (Cao et al., 1997; Ferrari et al., 1997; Walker & Korber, 2001), other studies have not shown this (Dorrell et al., 1999, 2001). Such studies require careful peptide titration experiments designed to reach physiologically relevant concentrations. Thus, unless vaccines can stimulate very strong T-cell responses to multiple epitopes, it is only prudent to match the vaccine immunogens to the circulating HIV clades in the target population (McMichael & Hanke, 2002).

Previously, we have constructed a DNA prime–modified vaccinia virus Ankara (MVA) boost candidate HIV vaccine expressing a common immunogen, designated HIVA (Hanke & McMichael, 2000). It is derived from consensus HIV-1 clade A Gag p24/p17 sequences and a string of clade A CTL epitopes; it does not contain the envelope gene and focuses solely on the induction of cell–mediated immune responses. In pre-clinical studies, both the pTHr.HIVA DNA and the MVA.HIVA vaccine components were highly immunogenic in mice and macaques (Hanke & McMichael, 2000; Wee et al., 2002). Reported here are small phase I clinical trials of this vaccine in healthy uninfected human volunteers in Oxford run under the auspices of the Medical Research Council of the United Kingdom (MRC) and the International AIDS Vaccine Initiative (IAVI).

METHODS

Regulatory approvals, volunteers and immunizations. The clinical studies were carried out in Oxford, UK and were approved by the Central Oxford Research Ethics Committee, the Health and Safety Executive, the Medicines Control Agency under the Doctors’ and Dentists’ Exemption certificate (DIX) and the Radcliffe Hospital Biological Safety Committee. The Gene Therapy Advisory Committee was notified. The vaccine trials were monitored by a Trial Steering Committee and Data Monitoring and Ethics Committee according to the MRC guidelines. Data were managed by the EMMES Corporation (Rockville, MD, USA).

HIV-uninfected males and females between 18 and 60 years of age who gave informed consent were screened, enrolled and immunized after giving further written informed consent to participate (further recruitment details can be found at http://www.oxavi.org/). All volunteers were assessed by experienced counsellors to be at low risk for HIV infection. For the pTHr.HIVA DNA-alone arm, six and 12 volunteers were randomized into two dosage groups to receive 100 μg (nos 01–06) or 500 μg (nos 07–18) of plasmid DNA, respectively, on days 0 and 21 by injection into alternate deltoid muscles. The volunteers and the clinical and immunological laboratory staff were blinded for the received DNA dose until all volunteers had passed day 189. The MVA.HIVA-alone arm was an open-label study, in which eight volunteers (nos 21–28) were injected intradermally with 5 × 107 p.f.u. of MVA.HIVA on days 0 and 21 into alternate arms. In the prime–boost study, nine volunteers (nos 02, 03, 04, 09, 11, 12, 14, 16 and 18) from the DNA study were boosted using the same dose of MVA, timing and route as in the MVA-alone trial at 9–14 months after the last DNA dosing. The volunteers who were boosted with MVA were chosen on the basis of willingness to re-enrol, not according to their immunological responses. All blood samples coming to the laboratory were coded.

Production of the pTHr.HIVA and MVA.HIVA vaccines. The pTHr.HIVA DNA and MVA.HIVA vaccines (Hanke & McMichael, 2000) were for the received DNA dose under Good Manufacturing Practice (GMP) conditions of COBRA Therapeutics (Keele, UK) (Williams et al., 1998) and IDT (Roßlau, Germany), respectively. The GMP vaccine batches were tested on their own and in the prime–boost protocol for toxicity, biodistribution and persistence in BALB/c mice in the Good Laboratory Practice facilities of Huntingdon Life Sciences (Huntingdon, UK) and showed no toxicity or evidence of persistence in any tissue other than at the site of injection at 5 weeks after the completion of dosing (Hanke et al., 2002). Thus, both vaccines were acceptable for use in phase I clinical trials as required by the UK Medicines Control Agency.

Isolation of peripheral blood mononuclear cells (PBMCs). Blood was drawn from healthy volunteers in vaccutainers containing preservative-free heparin. PBMCs were isolated from the whole
blood by Ficoll Hypaque cushion centrifugation using Lymphoprep 1.077 (Nycomed Pharma) as described previously. Cells were washed twice in RPMI [RPMI 1640 (Sigma-Aldrich) supplemented with glutamine and penicillin/streptomycin], counted and resuspended in R10 [RPMI supplemented with 10% fetal bovine serum (Sigma-Aldrich)] at \(2 \times 10^6\) cells ml\(^{-1}\). Isolated PBMCs were kept at 37°C and 5% CO\(_2\) until use.

**Preparation of peptide pools.** HPLC-purified peptides were purchased from Sigma-Genosys, with a purity of at least 80% by mass spectroscopy. Individual peptides were dissolved in DMSO (Sigma-Aldrich) to yield a stock of 10 mg ml\(^{-1}\) and stored at \(-80°C\). To prepare pools of 20–23 peptides (Fig. 1a), 20 μl of each peptide was combined and phosphate-buffered saline (PBS) was added to 5 ml. The pool was filtered, aliquoted, stored at 4°C and used within 1 week. For the assay, 10 μl of pooled peptides were added per well, so that each peptide was at a final concentration of 4 μg ml\(^{-1}\).

**The IFN-γ enzyme-linked immunospot (ELISPOT) assay.** A modified ELISPOT assay to detect peptide-specific release of IFN-γ was performed using fresh whole PBMCs. The assay had been

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**Fig. 1.** (a) A schematic representation of the HIVA immunogen which consists of consensus HIV clade A Gag p24/p17 sequences and a string of partially overlapping CTL epitopes. The peptide pools used in the IFN-γ ELISPOT assay are shown schematically below. (b) An example of electronically stored data from the IFN-γ ELISPOT assay. The plate is for pTHr.HIVA DNA-vaccinated volunteer no. 06, day 77 and illustrates the plate organization for whole fresh PBMCs. In addition to the HIVA-derived peptides, PHA and influenza virus/EBV/CMV (FEC)-peptide pool and no-peptide were used as positive and negative controls, respectively. On this assay plate, duplicate wells contained 200 000 (top two wells) and 100 000 (bottom two wells) cells.
validated showing good reproducibility when tested with HIV and influenza virus/Epstein–Barr virus (EBV)/cytomegalovirus (CMV) (FEC) peptide pools on appropriately immune volunteers (Mwau et al., 2002). Prior to the study, there were no responses to the HIVA-derived peptides in PBMCs of more than 50 unexposed uninfected volunteers (Mwau et al., 2002; and unpublished data). Our validation studies showed that there could be more than 50 % loss of response on freezing and thawing; therefore, the assays here were performed on freshly drawn PBMCs. Briefly, 96-well nitrocellulose-back plates (MAIP N4510; Millipore) were coated with 100 μl of an IFN-γ capture antibody (1 mg ml⁻¹; Mabtech) in PBS/0-01 % azide at room temperature for 4 h, washed six times with RPMI and blocked with 200 μl R10 for 1 h. Then, duplicates of 100,000 and 200,000 PBMCs for the DNA- and MVA-alone trials and quadruplicates of 200,000 PBMCs for the prime-boost trial suspended in 100 μl R10 followed by 10 μl aliquots of peptide pools were added into wells. The assay employed 87 15-aa-long peptides overlapping by 11 residues corresponding to the Gag portion of HIVA (pools 1–4) and 68 known CTL epitope peptides present in the HIVA polyepitope and Gag domains with a maximum of two mismatches according to the CTL epitope database (pools 5–7; Fig. 1a). Phytohaemagglutinin (PHA) and a pool of 21 peptides from influenza virus/EBV/CMV presented by common HLA types (FEC pool) were used as positive and no-peptide no-DMSO as negative controls. The schematic representation of HIVA and the whole PBMCs plate set-up are shown in Fig. 1(a, b), respectively. Plates were then incubated at 37 °C, 5 % CO₂ for 18 h, washed six times with PBS/0-05 % Tween 20 (Sigma-Aldrich), incubated with 100 μl of anti-IFN-γ-biotinylated detector antibody (1 mg ml⁻¹; Mabtech) in PBS/0-01 % azide at room temperature for 4 h and washed six times with PBS/0-01 % Tween 20. One-hundred microlitres of alkaline phosphatase-conjugated streptavidin was then added into each well at a dilution of 1:1000 in PBS, incubated at room temperature for 1 h and the plates were washed six times with PBS/0-01 % Tween 20. Finally, the IFN-γ ‘footprints’ were visualized by addition of 100 μl per well of a colour-development reagent (Bio-Rad) for 10–30 min, after which the plates were washed three times with cold tap water and dried overnight.

**ELISPOT data analysis.** Spot-forming units (s.f.u.) in the ELISPOT wells were counted by an automated ELISPOT reader (Autoimmun Diagnostika). Assay plates that did not meet quality criteria were discarded, i.e. if (i) there was no positive control response or (ii) the background in the no-peptide wells exceeded 100 s.f.u. per million PBMCs (20 s.f.u. per 200,000-cells well), although over 95 % of backgrounds were under 65 s.f.u. per million PBMCs. For the DNA, MVA and DNA–MVA boost trials, 75, 78 and 83 % of plates were accepted and the mean backgrounds in these assays were 36, 33 and 37 s.f.u. per million PBMCs, respectively. For calculations of peptide-stimulated responses, s.f.u. were determined from the 200,000-cell wells only. A response was considered positive if the peptide-pulsed cells gave frequencies of s.f.u. above the mean no-peptide background plus 2 standard deviations, i.e. positive with at least 95 % confidence, and the response was at least 50 s.f.u. per million PBMCs above the background. To calculate the mean responses for each time point, all responses (both positive and negative) for Gag overlapping peptide pools 1–4 and for known HIVA CTL epitope pools 5–7 were summed after subtracting the backgrounds to simplify the data presentation. Pools 1–4 and 5–7 were not added, to avoid possible counting of the same Gag-specific responses twice (see Fig. 1a).

**RESULTS**

**Safety**

Safety of the vaccines was a prime concern. The DNA vaccine was well tolerated with no local, systemic or laboratory serious adverse events. Long-term follow-up continues. The MVA gave small reactions at the site of intradermal injection; signs included erythema, induration and very small (1–2 mm) blister-like lesions that never coalesced or broke. The reactions subsided within 14 days. There were generally minimal systemic symptoms apart from in volunteer no. 23 in the MVA-alone trial, who developed a febrile illness with vomiting 1 day after the first MVA immunization. Because of low fluid intake the
volunteer was admitted for rehydration and rapidly recovered. It was not clear whether the adverse event was caused by the MVA vaccine. Subsequently, no similar reactions were seen in more than 100 volunteers (200 immunizations with the same MVA.HIVA at three trial sites; unpublished data). Detailed safety data will be published separately.

**T-cell responses to intramuscular pTHr.HIVA DNA**

Eighteen volunteers were vaccinated with either 100 or 500 μg of DNA and their T-cell responses were measured by frequency of fresh PBMC releasing IFN-γ in response to peptide stimulation *in vitro*. The overall pattern of responses is shown in Fig. 2(a). The results for summed responses specific for Gag (peptide pools 1–4) and known CTL epitopes in all of the HIVA immunogen, i.e., in the Gag and polypeptide regions (peptide pools 5–7; see Fig. 1a), are presented as an arithmetic mean ± standard error of all volunteer responses, positive and negative, at a particular time of the protocol (Fig. 2a) and varied in strength, ranging from 0 to over 900 s.f.u. per million PBMCs, hence the large standard errors of the mean. Maximum summed responses for each volunteer irrespective of time are also shown (Table 1). The HIV-specific responses were compared to no-peptide, and influenza virus/EBV/CMV peptide pool and PHA were used as negative and positive controls, respectively (not shown, for an example see Fig. 1b). Defining a positive response as one which is above the plate no-peptide background mean plus at least 2 standard deviations and at least 50 s.f.u. per million PBMCs above the background, the numbers of responders at each time point and the cumulative number of responders are shown (Fig. 2b). The responses to the DNA vaccine in responders were detected on average on 1.7 separate occasions and each volunteer responded to an average of 2.5 Gag pools (out of a maximum of four pools). For these small volunteer numbers, no differences were observed between the two doses of DNA. Surprisingly, HIV-specific responses were detected at 1 year after vaccination in seven volunteers, of which the stronger ones were confirmed on frozen cell samples. Otherwise, responses tended to peak 14–28 days after immunization. We were also able to identify several of the single peptides recognized by T cells of volunteers 05, 06 and 14 (not shown). According to our positivity criteria, a total of 14 volunteers responded to the DNA vaccination, of whom four and 10 received 100 and 500 μg doses, respectively.

**T-cell responses to intradermal MVA.HIVA**

The MVA.HIVA vaccine was also immunogenic. Similarly to DNA, the responses in fresh blood were variable ranging from 0 to over 1000 s.f.u. per million PBMCs (Table 1), of

### Table 1. Maximum positive responses for each volunteer

<table>
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<tr>
<th>Volunteer no.</th>
<th>DNA Gag (pools 1–4)</th>
<th>DNA Epitopes (pools 5–7)</th>
<th>DNA–MVA Gag (pools 1–4)</th>
<th>DNA–MVA Epitopes (pools 5–7)</th>
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<th>MVA Epitopes (pools 5–7)</th>
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<td>NR</td>
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</table>

NR, No positive response.

*Maximum summed responses in IFN-γ ELISPOT assay are shown as s.f.u. per million fresh PBMCs following stimulation with Gag (pools 1–4) and known CTL epitopes (pools 5–7). Counts in no-peptide background wells were subtracted. For each volunteer, and for the Gag and epitope data, the maximum responses were not necessarily detected at the same time points.
which the arithmetic mean ± standard error at a given time point are presented (Fig. 3a). Cumulatively, responses above the plate background mean plus 2 standard deviations and at least 50 s.f.u. per million PBMCs above the background were detected in seven out of eight volunteers (Fig. 3b). Five volunteers had HIV-specific responses still detectable at 1 year after vaccination. The responders had detectable responses in an average 3±1 blood samples taken throughout the study and each individual responded to an average of 2±4 Gag pools (out of four). There was no obvious boost after the second MVA.HIVA immunization.

Interestingly, volunteer no. 25 had a strong 1700 s.f.u. per million PBMCs response to peptide pool 2 on day 0, i.e. before immunization, which was maintained for at least 6 months (Fig. 3a). The response was shown to be mediated by CD8+ T cells recognizing the GQMREPRGSD (single letter amino acid code) peptide. This pool 2 response appeared to rise as the study progressed, possibly because responses were being made to other peptides in this pool of 22 Gag peptides. For this volunteer, the pool 2 response was excluded from the final analysis. The response to a single peptide before immunization is likely to reflect a cross-reaction to a single epitope in another antigen, possibly a persistent virus, although DNA database searches have so far failed to find a match other than for HIV Gag. Note that there is a possibility that a response could be induced purely through a conformational similarity, possibly with a different HLA molecule and a different peptide than those by which the response is detected (Lang et al., 2002). Because of the very low prevalence of HIV infection locally, the rigorous selection of low-risk volunteers and the fact that all volunteers were tested for HIV seronegativity at each visit during the trial, it is very unlikely that volunteer no. 25 was pre-exposed to HIV.

**T-cell responses to the pTHr.HIVA prime–MVA.HIVA boost regimen**

Nine of the DNA-primed volunteers were vaccinated with the MVA.HIVA 9–14 months after their last DNA immunization. The arithmetic means ± standard errors of all positive and negative responses detected by IFN-γ release at the time of the MVA vaccination, only one volunteer had detectable DNA-induced T-cell responses. Cumulatively, eight out of nine volunteers had responses higher than the plate background mean plus 2 standard deviations and at least 50 s.f.u. per million PBMCs above the background (Fig. 4b) with the highest frequency of over 2000 s.f.u. per million PBMCs (Table 1). On average, 3±2 responding blood samples per responder were identified and the average breadth of Gag-specific responses was 3±3 out of four Gag peptide pools. Given the fact that each pool may contain several peptides recognized by the vaccine-induced T cell, these results are encouraging.

**Antibody responses to HIV p24/p17**

Induction of antibodies against the HIVa p24/p17 domain was assessed in a standard ELISA assay. Of all volunteers enrolled in the three trials, only prime–boost volunteer no. 03 developed Gag-specific antibodies at the titre of 1/400 (not shown). This weak antibody immunogenicity may
facilitate the identification of HIV infections in possible future trials, which will enrol high-risk volunteers.

DISCUSSION

Within the limits of small numbers of volunteers in phase I studies, the safety and immunogenicity of the pTHr.HIVA DNA and MVA.HIVA candidate HIV vaccines were assessed and found to be encouraging. The vaccines on their own and in a DNA prime–MVA boost combination were safe and stimulated HIV-specific T-cell responses in the majority of volunteers.

The DNA vaccine provoked positive responses in 78% (n=18) volunteers. In general, the T-cell responses were fairly weak and transient. No differences were discernible between the 100 and 500 µg doses of DNA, both of which are regarded as low. Remarkably, using the same criteria of positivity, seven DNA-immunized volunteers showed T-cell responses after 1 year. These late responses were completely unexpected, as they had not been reported in previous DNA vaccine studies, but they have rarely been sought before. Using standard HIV diagnostic tests, we ruled out HIV infection as the cause of the late T-cell responses in DNA vaccine recipients. In addition, given the very low prevalence of HIV infection in the Oxford region and the rigorous selection of volunteers to be at negligible risk of HIV exposure, we think it is extremely unlikely that the responders had been exposed to HIV and somehow immunized. Also, because the responses were to more than one peptide pool, it is very unlikely that this represents a cross-reaction to some other intercurrent infection. The numbers of responders were small, however, and these late responses need to be sought and confirmed in future trials.

MVA.HIVA vaccination elicited HIV-specific T-cell responses in 88% (n=8) volunteers, of whom five had responses detectable at 1 year after vaccination. As anticipated, the MVA-induced responses were stronger and more frequently detected than those elicited by DNA. Similar results were seen in macaques immunized with recombinant MVA (Seth et al., 1998) and in human volunteers immunized with a recombinant canarypox vaccine (Cao et al., 2003).

The pTHr.HIVA prime–MVA.HIVA boost protocol induced responses in 89% (n=9) volunteers. As far as it can be inferred from these small numbers of volunteers, responses elicited by the DNA prime–MVA boost regimen were very similar in the whole PBMCs to those induced by MVA alone. Preliminary studies showed a difference in the frequencies of non-CD8+—presumably CD4+—T-cell responses, which were estimated by a magnetic-dynabead depletion of CD8+ cells (not shown). These experiments suggested that better non-CD8+ responses were observed for the DNA and especially prime–boost vaccinations compared to MVA alone. Similar observations were made in the trial of candidate vaccines for malaria (McConkey et al., 2003). Generation of HIV-specific CD4+ T-cell responses would be encouraging, because it could facilitate stimulation of a better quality immune response than that elicited during natural HIV infection, and needs to be explored in future studies. In healthy HIV-uninfected volunteers, CD8+ T cells are primed in the presence of intact CD4+ help and therefore may be more efficient when facing the incoming HIV (Janssen et al., 2003).
Higher frequencies of responders to the vaccination were detected in these three trials than seen previously (Ugen et al., 1998; Wang et al., 1998; Boyer et al., 2000; MacGregor et al., 2002; McConkey et al., 2003). A number of circumstances could have contributed to this. First, fresh rather than frozen-and-thawed cells were used throughout the trials and during the validation of the IFN-γ ELISPOT assay – fresh cells gave two- to threefold higher frequencies (Mwau et al., 2002). Second, different and possibly less-sensitive assays were employed in previous trials. Third, the IFN-γ ELISPOT assay can be desensitized in an attempt to decrease the background no-peptide counts (E. G.-T. Wee, A. J. McMichael & T. Hanke, unpublished data), which may be genuine and caused by a reactivated CMV infection (Dunn et al., 2002). It was noted that the IFN-γ spots generated by the vaccine-induced T cells were much smaller compared to the ones produced by PHA and well-established responses to chronic viral infections such as the influenza virus/EBV/CMV (Fig. 1b) or indeed HIV (Mwau et al., 2002). This might indicate, that in vaccine trials, responses that are being freshly induced and measured during the course of the trial are qualitatively different from those observed in HIV-infected people which are often used for validation of trial assays. This could also explain the ‘apparent’ transient nature of these responses, their different resistance to freezing–thawing procedures and sometimes marginal functionality. Experiments addressing these issues are under way. The significance of IFN-γ production for the defence against HIV infection is not clear; other T-cell functions may be more relevant and should be explored in future. Ultimately, efficacy can only be shown in a phase III trial in humans. Therefore, the most encouraging observation in these trials is the high frequency of individuals whose T-cell responses were primed to a number of HIV epitopes.

At this stage, it is important to advance the progress of vaccines that can stimulate strong and specific T-cell responses to a proof-of-principle or efficacy trial as quickly and safely as possible. The pTHr.HIVA and MVA.HIVA vaccines by virtue of their initial immunogenicity in human trials described here look promising, but there is still some way to go.

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Vaccine-induced HIV-specific T cells in humans


