Highlights from the HIV Research for Prevention Conference (R4P), 17–21 October 2016, Chicago, IL, USA

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Introduction

The HIV prevention research community gathered in Chicago, Illinois, USA for the second biennial HIV R4P, the only scientific conference dedicated to biomedical HIV prevention research. The conference highlighted advances in preventive HIV vaccines, updates on oral PrEP, advances in mucosal immunology and sequencing, and updates on the role of monoclonal antibodies in pathogenesis and transmission. Finally, a satellite meeting on systems biology and vaccines highlighted the systems-based approaches utilised to accelerate vaccine development.

HIV preventative vaccines

Sandhya Vasan

The HIV Research for Prevention Conference (R4P) showcased many advances in preventive HIV vaccines. Several trials built upon RV144, the only trial to date to demonstrate partial efficacy of a preventative HIV vaccine [1]. The RV305 trial in Thailand administered two boosts of ALVAC-HIV, AIDSVAX® B/E protein, the combination, or placebo, 6–8 years post initial vaccination of RV144 vaccine recipients, whereas RV306 enrolled naive participants in Thailand to receive the RV144 regimen or placebo, followed by boosting in various intervals. Siriwat Akapirat presented data demonstrating that IgG binding titers to gp120 A244, gp120 MN, and V1V2 scaffolds increased with boosting in RV306 both in plasma [2], cervicovaginal, rectal and seminal secretions [3], accompanied by increases in Tier 1 neutralisation responses in RV305 and RV306 presented by Lindsay Wieczorek [4] and HIV-1 Env-specific IgG producing plasmablasts in RV306, presented by Alexandra Schuetz [5]. While these responses were equivalent in subjects boosted with either AIDSVAX® B/E protein alone or in combination with ALVAC-HIV, Carolina Herrera found that transcriptional responses to cervical explants from RV305 vaccines differed between these groups [6]. In addition to cellular and humoral responses, innate mechanisms may play a role. Michael Eller [7] described natural killer cell activation following late boosting in RV305. Stephen Kent emphasised not only the role of antibody-dependent cellular cytotoxicity (ADCC) in protection in RV144, but the importance of interactions of antibodies with other molecules such as neutrophils [8]. Building from the work in Thailand, the Pox Protein Public Private Partnership (P5) is exploring the potential of a potential paediatric DNA/MVA vaccine regimen that induced HIV env-specific antibodies particularly in an extended interval group [9]. The goal is to target infants of HIV-infected mothers to protect from oral breastmilk transmission.

Lindsay Baden presented data from a Phase 1 trial evaluating two MVA constructs with mosaic inserts that spanned biologically engineered HIV-1 sequences designed to maximise global coverage across HIV-1 subtypes. Vaccines were administered to healthy adults who were either naive or who had received adenovirus type 26 (Ad26) EnvA 4–6 years earlier, who had persistent detectable anti-Env responses. All vaccines were safe and well-tolerated, and MVA elicited cross-clade ELISPOT and ELISA responses in both groups [20]. A similar NHP study presented by Frank Wegmann evaluated the relative efficacy of Ad26 mosaic regimens with or without MVA mosaic vaccines and/or Clade C gp140 protein against intrarectal SHIV162p3 challenge. Groups receiving Ad26 had higher HIV-1 specific IFNγ ELISPOT responses, whereas groups receiving the gp140 protein boost had higher anti-gp140 ELISA responses. Overall, Ad26 prime, Ad26+gp140 boost showed the highest efficacy at 66% full protection after six challenges [21]. Other novel vaccine regimens in the pipeline include intranasal Sendai virus vector followed by intramuscular adenovirus-35 (Ad35).

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antigen-specific T-cell subsets (COMPASS) scores was inversely associated with risk of HIV acquisition [11].

Data from HVTN 096/EV04 presented by Giuseppe Pantaleo [12] demonstrated that simultaneous co-administration of either NVYAC or DNA vaccines expressing subtype C Env, Gag and Pol-Nef with the AIDSVAX® B/E protein affords a more rapid induction of immune responses, which would be important for early coverage of high-risk individuals. The magnitude or humoral and cellular responses and durability of humoral responses was also improved, findings corroborated in studies of DNA-protein vaccine co-administration in HVTN105 were presented by Nadine Rouphael [13] and in non-human primates (NHP) were presented by Barbara Felber [14].

Several trials utilised the DNA-prime, modified vaccinia Ankara (MVA)-boost regimen. Agricola Joachim [15] presented data showing that multi-plasmid DNA prime followed by HIV-MVA-CMDR boost in Tanzanian volunteers induced frequent and durable antibody and T cell responses. A trial in Mozambique presented by Edna Viegas determined that delivery of the DNA prime via intradermal electroporation did not increase the magnitude of responses over intradermal (ID) injection alone. Incorporation of the GLA adjuvant, a TLR4 agonist, improved binding antibody responses, and boosting with MVA improved Tier 1 homologous neutralising antibody responses [16]. Utilisation of the CM-CSF adjuvant in the GeoVax DNA/MVA vaccine regimen preferentially improved durability of anti-gp1 antibodies over gp120 antibodies in HVTN094 [17]. In contrast, UK HVC 033, a DNA/MVA clinical trial with different inserts and GLA adjuvant showed preferential anti-V3 responses over gp41 [18]. Thus, inserts, schedule and adjuvants all play a role in influencing the immunogenicity of various vaccine regimens. Finally, Bonnie Philips presented the exploration of a potential paediatric DNA/MVA vaccine regimen that induced HIV env-specific antibodies particularly in an extended interval group [19].

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in humans [22], replicating cytomegalovirus vector (CMV) [23] in NHP, and full length single chain gp 129-cd4 (FLDC), a fusion protein consisting of a modified full-length gp120 protein, linked to the first two domains of human CD4, in NHP [24]. In addition to novel vaccines, Sudhir Kasturi suggested that the TLR 7/8 ligand 3MO52, when used as an adjuvant alone or in combination with GLA, improved the magnitude and durability of humoral and T-follicular helper cell responses to an HIV-Env protein antigen in NHP [25].

Pre-exposure prophylaxis (PrEP)
Tanyaporn Wansom
In the opening plenary, Myron Cohen highlighted novel agents and mechanisms for prevention such as long-acting injectable ARV preparations including rifampirine, an NNRTI, and cabotegravir, a long acting integrase inhibitor, which will be directly compared to tenofovir in HPTN 083 and 084 to prevent HIV acquisition in men who have sex with men (MSM) and transgender women (TGW) [1]. Sharon Hillier shared findings from the MTN-020 ASPIRE trial where dapivirine containing vaginal rings were found to reduce HIV acquisition in women (27% reduction in primary ITT analysis, 95% CI 1–46; P=0.046). She stressed that adherence strongly predicted effectiveness; in the MTN-020 ASPIRE trial, the efficacy differed significantly according to age, with efficacy of 61% (95% CI 32–77; P=0.001) among women 25 years of age or older and 10% (95% CI −41–43; P=0.64) among those under the age of 25 years [2]. Maria Husnik presented data showing that providing feedback to sites regarding real-time site-level drug levels in a way that preserved blinding led to increased adherence among participants [3]. Finally, Urvi Parikh found no difference in the rates of NNRTI-associated mutations in study seroconverters exposed to dapivirine compared to placebo [4].

Susan Ford presented data from the ÉCLAIR study characterising the PK tail in people receiving long acting (LA) cabotegravir, with 17% of participants having quantifiable CAB levels at 52-weeks post injection-3, raising the potential for virological resistance and the need for alternative HIV prevention methods following the discontinuation of CAB LA as PrEP [5]. Deborah Donnell described the course of the seroconversion process in the Partners PrEP study comparing those assigned to an active PrEP strategy (TDF alone or TDF/FTC) to placebo-treated seroconverters in serodiscordant heterosexual couples, finding no statistically significant difference in progression through the Fiebig stages; however, an approximate 30% delay in progression through Fiebig stages 5 and 6 (detection by confirmed Western Blot) was associated with actual PrEP use [6]. In the Partners Demonstration Project, Maria Pya presented data that women in serodiscordant couples had high adherence to PrEP based on MEMS cap data, with women taking six or more doses of PrEP for 77% of weeks [7]. Alex Carballo-Dieuguez presented the results of MTN-017, showing, via a mixed methods analysis, good acceptability and high levels of adherence to a rectal microbicide tenofovir gel (both daily and at times of receptive anal intercourse), comparable to levels of adherence achieved using oral TDF/FTC [8].

Albert Liu reported that young MSM and TGW aged 18–29 had high PrEP uptake in Chicago, with 70% of participants providing dried blood spot at week 4 of PrEP, and 92% of those with TFV-DP levels consistent with taking ≥4 doses a week [9]. Susan Scheer presented data on PrEP users in San Francisco through Kaiser Permanente (KPSF) and SF Public Health Funded Primary Care Clinics; >90% of users were men and most were white and 30–39 years; in comparison, 45% of newly diagnosed HIV cases in SF, in 2014, were white, and 30% were 30–39 [10]. Robyn Eakle reported that uptake and use of PrEP by female sex workers in South Africa has been promising, with high uptake among those eligible (90%) but variable retention (40–90%); no seroconversions have been reported in the PrEP arm, and there was no change in reported condom use over the period of the study [11].

References
All abstracts, posters and symposiums were presented at HIV Research for Prevention 2016. October 2016, Chicago, USA. Available from: http://hivr4p.org.
1. Cohen M. ART prevents HIV transmission: what happens next? Poster PL01.01.
2. Hillier S. Rings and things. Poster PL03.03.
3. Hussnik MJ, Brown E, Marzinke M et al. Novel implementation of a real-time adherence monitoring strategy within a Phase III, blinded, placebo-controlled, HIV-1 prevention clinical trial. Abstract OA20.05.
4. Paskh LM, Halvorsen E, Magaret CA et al. HIV-1 resistance outcomes in seroconverters from the MTN-020/Aspire dапивіріне vaginal ring study. Abstract OA03.03.
5. Ford S, Stancil B, Markowitz M et al. ECLAIR study of cабогтрілграв LαІінікшо: characterization of safety and PK during the “PK Tail” phase. OA12.06LB.
6. Donnell D, Ramos E, Baten J et al. The effect of oral pre-exposure prophylaxis on the progression of HIV-1 seroconversion. Abstract OA03.01.
7. Pyra M, Helfson R, Haberer J et al. PrEP adherence among East African women with HIV-infected partners participating in an open-label study. Abstract OA16.02.
8. Carballo-Dieguez A, Balan I, Giguere R et al. High levels of adherence to a rectal microbicide gel and to oral PrEP achieved in MTN-017. Abstract OA20.01.
9. Liu A, Vittinghoff E, von Felten P et al. Initiation and early adherence among young MSM and transgender women in Chicago in the enhancing PrEP community (EPIC). OA16.01.
10. Scheer S, Scott H, Marcus J et al. PrEP uptake and demographic characteristics of PrEP users in two large medical systems in San Francisco. OA24.03.
11. Eakle R, Gomez G, Mbogua J et al. Treatment and prevention for female sex workers in South Africa: first-year results for the TAPS demonstration project. Poster PDO4.02LB.

Mucosal immunology

Alexandra Schuetz

Profound and durable suppression of HIV by antiretroviral therapy (ART) represents a major accomplishment in HIV/AIDS research. However, successful attempts to induce sustained virological remission following ART withdrawal have been limited. James Arthos [1] and Claudia Cicala [2] reported on a study, recently published in Science, by Byrareddy et al. [3] that the gut-homing Integrin α4β7, is linked to pathogenesis, persistence and prevention. In a non-human primate (NHP) model, infection with SIV, followed by suppressive ART with co-administration of a monoclonal antibody (mAb) to α4β7, then subsequent withdrawal of all treatment, resulted in viral suppression, lower pro-viral DNA in gut mucosa associated lymphoid tissue (GALT) and restoration of mucosal CD4 T cells. The mechanism by which α4β7 mAb promotes the observed prolonged virological control and CD4 T cell restoration is not understood yet, but has been linked to the recovery of mucosal Th17 and Th22 subsets and a significant increase in cytokine-producing NK cells and NKp44+ ILCs. This data paved the way for a proof of concept study in 15 HIV-infected patients using Vedolizumab, a human α4β7 mAb already used to treat inflammatory bowel disease.

Aida Sivro [4] presented additional data highlighting the importance of the gut-homing Integrin α4β7 during HIV acquisition in the context of CAPRISA 004. The expression of β7,α4 on peripheral CD4 T cells was associated with higher HIV acquisition, higher viral load and faster disease progression, remaining significant in a multivariate model. She hypothesised, that a higher frequency of β7,α4 CD4 T cells leads to increased viral replication at the site of exposure and rate at which the virus spreads to the GALT where it encounters a large number of susceptible target cells.

Data from CAPRISA 004 also showed the importance of the vaginal microbiome in the context of a PrEP efficacy trial [5]. Using a proteomics approach to identify the vaginal microbiota he observed, that in women with Lactobacillus iners dominance, indicative for a healthy microbiome, tenofovir efficacy was 3-fold higher than in women with vaginal dysbiosis (61% vs 18% efficacy, respectively). Upon further investigation, Gardnerella vaginalis, dominant in women with vaginal dysbiosis, was found to rapidly deplete tenofovir while this was not the case for L. iners. This identifies a mucosal signature that relates to a novel putative mechanism contributing to the lower efficacy of tenofovir. In conjunction with host inflammatory and epithelial barrier effects, this may pose a multifactorial mechanism contributing to lower efficacy and might be taken in consideration for other trials and drugs.

In non-human primates, a study by Alexandra Ortiz [6] demonstrated that ART contributes to intestinal immune dysfunction by potentially modifying the microbiome in healthy macaques. This is one of the first studies investigating ART-associated changes of the microbiome and its subsequent immunological effects. After treatment with ART (daranavir/ritonavir) for 7 days, they observed a change in the microbiome towards dysbiosis with an increase in Proteobacteria, known to be associated with ongoing immune activation and depletion of mucosal Th17 and Th22 cells, at the expense of Bacteroidetes. In addition, they observed changes in mucosal CD4 and CD8 T cell function and phenotype. Even though this was a small study with a limited course of treatment, these results warrant further studies.

Taken together, this meeting has highlighted the importance of the mucosal barrier housing most of the body’s lymphocytes as well as mucosa associated microbiome containing viruses, bacteria, archaea, fungi and other eukaryotic organisms and their interactions in the context of HIV pathogenesis, persistence and prevention.

References

All abstracts, posters and symposiums were presented at HIV Research for Prevention 2016. October 2016, Chicago, USA. Available from: http://hivr4p.org.

1. Santangelo P, Byrareddy S, Cicala C et al. Immuno–PET/CT imaging reveals differences in virus and CD4+ cell localization in SIV infected rhesus macaques treated with an anti-α4β7 mAb. HIV research for prevention. Abstract OA07.02.
2. Cicala C. A Central Role for α4β7+ CD4+ T Cells in HIV Transmission and Pathogenesis. HIV Research for Prevention. Symposium SY02.01.
3. Byrareddy SN, Arthos J, Cicala C et al. Sustained virologic control in SIV+ macaques after antiretroviral and alphabeta7 antibody therapy. Science. 2016, 354: 197-202.
4. Sivro A, Yende N, Leahk K et al. The role of gut homing receptor α4β7 in HIV pathogenesis and transmission – a prospective cohort study. Abstract OA07.01.
5. Burgerer A. Vaginal bacteria modulate HIV pre-exposure prophylaxis efficacy in women. Symposium SY02.04.
6. Ortiz A, DiNapoli S, Sortino O et al. Antiretroviral therapy contributes to intestinal immune dysfunction in healthy macaques. OA07.05.

A central role of α4β7 in HIV pathogenesis and transmission

Shelly Krebs

A common thread of presentations pertaining to the role α4β7 in pathogenesis and transmission started the opening plenary session with a talk given by Anthony Fauci. He revealed groundbreaking data from a recently published article in Science by Byrareddy et al. that demonstrated a monoclonal antibody (mAb– Vedolizumab) targeting α4β7 was able to control viral load to low or undetectable levels and normalise CD4 T cell counts in plasma and mucosal tissues for more than 9 months in SIV-infected macaques, even after ART was withdrawn [1]. The expression of α4β7 on immune cells homed lymphocytes to effector sites in the large and small intestine, and several lines of evidence suggest that the gastrointestinal mucosa play a critical role in HIV pathogenesis. CD4 T cells are rapidly depleted from this site during the first weeks of infection. The absence of regulatory T cells within the gut mucosa has been shown to increase microbial translocation of bacterial products resulting in sustained immune activation, a hallmark of chronic HIV infection. Subsequent presentations by Aida Sivro and Claudia Cicala, revealed CD4 T cells expressing α4β7 were depleted from the peripheral blood and colon within the first
2 weeks f HIV infection and are not restored after 6 months even when ART is initiated at this early stage. However, CCR5+ CD4+ cells were not depleted until Fiebig III, suggesting that α4β7-expressing CD4 T cells maybe the early preferred target of HIV infection. Previous studies have shown that CD4 T cells expressing α4β7 bind directly to HIV Env, specifically to the V2 loop. Although α4β7 has not been unequivocally demonstrated as a receptor of HIV, the ability of α4β7-expressing T cells to bind to HIV Env and migrate to the gut may reveal a mechanism in the early days of HIV infection for viral dissemination. In addition, Aida Sirvio revealed results that higher integrin β7-Hi expression on peripheral CD4 T cells prior to infection is associated with higher rates of HIV acquisition, increased VL, and faster disease progression. Finally, in a nonhuman primate model of transmission an anti-α4β7 mAb protected macaques from mucosal transmission of SIV. These results demonstrate an important role for α4β7 in HIV pathogenesis and transmission.

Targeting of HIV Env with mAb in treatment interruption studies has become a strategy used in many studies to try to diminish the HIV reservoir. Targeting a gut homing receptor on CD4 T cells prior to infection is associated with higher rates of HIV acquisition, increased VL, and faster disease progression. Finally, in a nonhuman primate model of transmission an anti-α4β7 mAb protected macaques from mucosal transmission of SIV. These results demonstrate an important role for α4β7 in HIV pathogenesis and transmission.

Reference
1. Byrareddy SN, Arthos J, Cicada C et al. Sustained virologic control in SIV+ macaques after antiretroviral and alpha4beta7 antibody therapy. Science 2016; 354: 197–202.

Systems biology and vaccines
Rasmi Thomas

The systems biology and vaccines satellite meeting at the HIVR4P conference highlighted systems-based approaches to accelerate vaccine development. Rafick Sekaly from Case Western University described efforts to identify correlates of immunogenicity and protection triggered by vaccines using an integrative meta-analysis of data obtained from transcriptomics, cytokine profiling, haematology and flow cytometry [1]. Elias El Haddad from the University of Drexel, PA, USA used a systems biology approach to identify novel adjuvants that can potentially boost follicular helper T cell function and change the quality of the antibody response. They have also identified multiple metabolic pathways that will be targeted for vaccine development including against HIV.

Bali Pulendran, Emory University presented an elegant overview of systems vaccinology, and discussed the initial studies from his laboratory, which provided proof of concept of the utility of systems approaches in delineating molecular signatures of vaccine immunity, with yellow fever, influenza and meningococcal vaccines [2–4]. He noted that systems based approaches are rapidly becoming an integral component of immune monitoring in vaccine trials. However he underscored the importance of going beyond signatures, and of extracting knowledge and biological insight from the vast body of data that is being rapidly generated. In this regard he highlighted emerging biological insights, such as the central role of the ancient amino acid sensing pathway involving the molecule GCN2 in immune regulation [5,6], which emerged as a result of systems vaccinology in humans. Finally, he concluded by discussing the potential of systems approaches to delineate signatures of vaccine efficacy in the context of a malaria vaccine trial in humans. These findings add to the growing evidence of the role of two domain Killer Immunoglobulin-like receptors and susceptibility to malaria.

Julie McElrath from the University of Washington discussed preparations by their group to integrate systems biology in the HTVN vaccine trials. Scott Handley from the Washington University reviewed recent findings showing that SIV infection mediated expansion of the gut virome can be prevented by the Ad26/Env vaccine regimen [7]. Handley also described their efforts in collaboration with the Ragon Institute in Boston to identify differences in microbiomes of acutely HIV-1 infected individuals from the FRESH cohort in South Africa. They observed significant differences in the female genital tract bacterial microbiome and virome of HIV-1 infected women.

References
1. Kuri-Cervantes L, Fourati S, Canderan C et al. Systems biology and the quest for correlates of protection to guide the development of an HIV vaccine. Curr Opin Immunol 2016; 41: 91–97.
2. Querec TD, Akondy RS, Lee EK et al. Systems biology approach predicts immunogenicity of the yellow fever vaccine in humans. Nat Immunol 2009; 10: 116–125.
3. Nakaya HI, Wrammert J, Lee EK et al. Systems biology of vaccination for seasonal influenza in humans. Nat Immunol 2011; 12: 786–795.
4. Li S, Roupaha D, Duraisingham S et al. Molecular signatures of antibody responses derived from a systems biology study of five human vaccines. Nat Immunol 2014; 15: 195–204.
5. Ravindran R, Khan N, Nakaya HI et al. Vaccine activation of the nutrient sensor GCN2 in dendritic cells enhances antigen presentation. Science 2014; 343: 313–317.
6. Ravindran R, Loebermann J, Nakaya HI et al. The amino acid sensor GCN2 controls gut inflammation by inhibiting inflammasome activation. Nature 2016; 531: 523–527.
7. Handley SA, Desai C, Zhao G et al. SIV Infection-Mediated Changes in Gastrointestinal Metabolic Pathways Prevented by Vaccination. Cell Host Microbe 2016; 19: 323–335.

Sequencing
Gustavo Kijak

The study of HIV-1 genetics and evolution can provide important information about the bottleneck that follows mucosal transmission, the pathways exploited by the virus to escape antibody responses during natural infection, and the selective pressure exerted by vaccination. During the HIV Research for Prevention 2016 conference, these topics were addressed by several presentations.

Klein et al. [1] used next-generation sequencing (NGS) to compare genetic diversity in the HIV-1 C2-V3 region in plasma versus endocervical swab samples obtained from 80 women from Uganda and Zimbabwe within 7 months of infection. They found a significantly higher genetic diversity in the female genital tract (FGT) than in blood. When comparing the samples from the same compartment obtained <3 months (acute) versus 3–7 months (early) post infection, they found contrasting profiles. In the FGT, acute samples had a higher genetic diversity than early samples, whereas in plasma, acute samples had a lower genetic diversity than early samples. These differences remained significant regardless of viral subtype.

Macharia et al. [2] presented the molecular characterisation of acute infection among 19 men having sex with men (MSM) from Kenya. They performed NGS of full-length viral genomes and found that 37% of the participants were infected with unique recombinant forms. The authors reported that 32% of the participants were infected with >1 transmitted/founder (T/F) virus, and this group presented markers associated with negative clinical outcomes (higher acute infection plasma viral load and lower CD4 cell counts at later time points).

V3 glycan dependent immunogens are a major focus of vaccine development, and Anthony et al. [3] presented their study of HIV-1
escape from strain-specific antibodies (ssAb) versus broadly neutralising antibodies (bNAbs) targeting this epitope using next-generation sequencing (NGS). Participant CAP177 from the CAPRISA 002 cohort had developed an early ssAb response against the V3/C3 region, from which the virus rapidly escaped. Later, a bNAb response emerged, targeting the N332 supersite, which was also followed by viral escape, but at a slower rate. The authors detected major differences in the mutational pathways for escape from the two responses: escape from the early ssAb response developed through a replacement of N-glycosylation (334 to 332), while escape from the bNAb response developed through combined replacement of N-glycosylation (332 to 334) and increases in V1 loop length and glycosylation content. Overall, these results support the complexity of the mutations required for loss of viral sensitivity to bNAbs may impose a higher barrier for viral escape from these responses.

Finally, de Camp et al. [4] presented the sieve analysis of breakthrough infections in the Phase IIb HIV-1 vaccine study HVTN 505. Even though the vaccine study had not shown efficacy, the analysis of viral sequences from 27 vaccine and 20 placebo recipients showed significantly higher numbers of mismatches against the vaccine insert in the CD4-binding site in vaccine recipients. These results support vaccine-induced selective pressure.

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References

1. Klein K, Nickel G, Nankya I and Arts E. Higher HIV-1 envelope sequence diversity in the vaginal tract than in blood at early stage of infection. Abstract OA18.04.
2. Macharia G, Yue L, Dernela D et al. Transmission of multiple HIV-1 founder viruses and high frequency of unique recombinant forms among MSM in Kenya. Abstract OA18.03.
3. Anthony C, York L, El-Badry E et al. Viral escape from HIV broadly neutralising antibodies. Abstract OA01.04.
4. de Camp A, Rolland M, Edlefsen PT et al. Sieve Pressure toward the CD4 Binding Site of Env in HVTN 505 Breakthrough Infections. Poster P12.03.