

Discussed posters

DP1

HIV-2 interaction with macrophages and dendritic cells

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In the last decade many advances have been made in understanding how HIV-1 interacts with macrophages (MØ) and dendritic cells (DC). Based on the notion that HIV-2 is a more attenuate model of infection, we proposed to explore the mechanisms of HIV-2 interaction with MØ and DCs.

With this aim, we studied the efficiency of cis-infection of MØ and DCs. A cohort of 7 HIV-1 and 7 HIV-2 primary isolates were chosen based on coreceptors usage profile and on the clinical/immunological stage of infection.

MØ, immature monocyte-derived DCs (IM-MDDCs) and mature monocyte-derived DCs (M-MDDCs) were obtained from healthy donors and infected with different HIV-2 and HIV-1 primary isolates or left uninfected as controls. Virus production was monitored by reverse transcriptase (RT) activity. We also analyze integrated viral DNA in exposed cells by amplification of LTR region by a nested-PCR technique to evaluate the ability of each viral isolate to enter cells and to perform initial events of replication cycle.

In HIV-2, viral replication on MØ was detected in 4 viral isolates. Two of them were also able to replicate both in IM-MDDCs and M-MDDCs. Regarding HIV-1 infection, only one isolate was able to productively infect MØ. This isolate and another one replicate in IM-MDDCs while none of the HIV-1 tested were able to replicate in M-MDDCs.

We further assessed the proviral DNA integration in different cell populations. We observed that one HIV-1 isolate did not integrate its proviral DNA into IM-MDDCs and M-MDDCs host-cell DNA. All the other isolates had integrated their genome.

Our results suggest that the ability to infect MØ or DCs is independent on virus phenotype and did not correlate with clinical/immunological stage of the patient. Furthermore, HIV-2 infection of MØ and DCs seems to be more frequently observed than in HIV-1. Finally, there is clear evidence that reverse transcription and integration occurs even in those isolates for which there was no RT activity detection.

DP2

Soluble ST2 rings the alarm for gut damage and immune activation in primary HIV infection

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Introduction: Following breaches of the tissue barrier or infection, interleukin-33 (IL-33) is released as an alarmin to induce inflammation. sST2, the soluble isoform of the IL-33 receptor, acts as a decoy receptor to prevent systemic inflammation. We assessed relationship between the IL-33/ST2 axis and gut mucosal damage markers in patients with early HIV infection (EHI).

Materials and methods: We measured IL-33 and sST2 plasma levels in patients with EHI ($n=48$), chronic HIV infection (CHI; $n=61$) and in elite controllers ($n=21$); and prospectively in sub-groups of patients. We assessed potential correlations between ST2 levels and plasma viral load (VL), CD4 and CD8 T-cell counts, the expression of T-cell activation (HLADR/CD38) and exhaustion (PD-1), gut epithelial damage (I-FABP), inflammation (IFN- β , IL-6) and microbial translocation (LPS, sCD14) markers and Kynurenine/Tryptophan (K/T) plasma levels.

Results: IL-33 plasma levels were at the limit of detection in all groups, while plasma sST2 levels were elevated in EHI (18,538 pg/mL, $P<0.001$) and in CHI (15,115 pg/mL, $P=0.044$) compared to uninfected controls (11,684 pg/mL). In EHI, plasma sST2 levels were positively correlated with the CD8 T-cell count ($r=0.289$; $P=0.045$) and with the percentage of T-cells expressing activation and exhaustion markers ($P<0.05$), but not with VL or CD4 T-cell count. Plasma sST2 levels also correlated with the levels of I-FABP, sCD14, sCD40L, IFN- γ and with the K/T ratio ($P<0.05$). Prospective analyses of EHI showed that early antiretroviral therapy had no impact on plasma sST2 levels, while longer treatment duration initiated during CHI resulted in normalized sST2 levels ($P<0.001$).

Conclusions: Since sST2 levels were elevated in early HIV infection and were correlated with CD8 T-cell count, immune activation and microbial translocation, sST2 may serve as a marker of disease progression and gut damage. The IL-33/ST2 axis may contribute to gut damage in persistent viral infection.

DP3

10E8V2.0/iMab: an engineered membrane-anchored bispecific anti-HIV antibody effective in preventing and treating HIV in humanized mice

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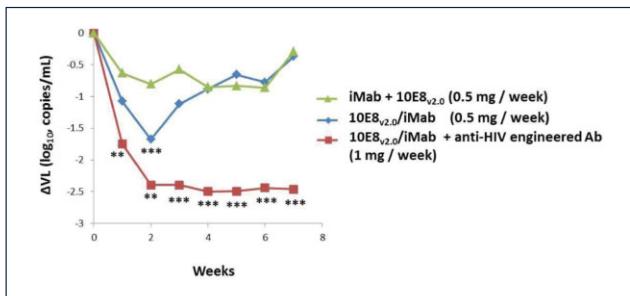
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The emergence of a new generation of virus-neutralizing monoclonal antibodies (Abs) has re-ignited the field of passive immunization as an alternative strategy for HIV prevention. Here, we report the impressive *in vitro* and *in vivo* activity of an engineered bispecific Ab.

The CrossMab technology was used to construct a library of bispecific Abs. One potent and broad Ab, 10E8V2.0/iMab, was identified, with one arm targeting the human CD4 receptor using ibalizumab (iMab) and the other arm targeting gp41 using a modified 10E8 (10E8V2.0). First, humanized NSG mice infected with HIV JR-CSF received weekly injections of 0.5 mg 10E8V2.0/iMab for 7 weeks, alone or in combination with 0.5 mg of an anti-gp120 engineered Ab. Second, uninfected mice receiving weekly injections of 0.2 mg 10E8V2.0/iMab were challenged 3 times intraperitoneally with JR-CSF.

10E8V2.0/iMab showed breadth of 100% against a panel of 118 HIV strains, with mean IC50 and IC80 of 0.002 ug/mL and 0.006 ug/mL, respectively. *In vivo*, this Ab alone reduced the virus load by 1.7 log in infected mice after 2 weeks of treatment. Subsequent viral rebound was associated with mutations in the 10E8 epitope, implying that its antiviral activity was mainly mediated by the 10E8V2.0 arm that is concentrated at the site of viral entry. The combination of 10E8V2.0/iMab and an anti-gp120 Ab led to a sustained viral load decrease of 2.3 log during the course of treatment. 10E8V2.0/iMab alone also provided complete protection in humanized mice against three systemic HIV challenges, whereas 16/19 saline-treated mice became infected after one challenge.

10E8V2.0/iMab appears to be the most potent HIV-neutralizing Ab described to date. It has shown unprecedented activity for an Ab in both treating and preventing HIV in a humanized mouse model. It could potentially serve as an anchor for a combination of antibodies as long acting regimen for HIV treatment.

**Figure DP3.1.** Therapeutic efficacy of 10E8V2.0/iMab** $P < 0.01$, *** $P < 0.001$ as determined by Mann-Whitney test.

DP4

Factors associated with voluntary HIV testing uptake among young people in Saudi Arabia

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Background: Despite recent progress in enhancing the accessibility of HIV-related health services worldwide, opportunities to diagnose patients are often missed due to genuine barriers at different levels. The aim of the study is to explore the factors that affect the utilization of HIV testing services by young people in Saudi Arabia.

Methods: An explanatory sequential mixed methods was used to reveal the factors that influenced HIV testing among young people aged 17–25 years. For the quantitative strand of the study self-completed questionnaire was used and the study sample was drawn using a convenience sampling technique. Then, a semi-structured interviews were used to gather the perspective of healthcare professionals working in the field of HIV/AIDS in the country.

Results: 394 participants completed the questionnaires 116 (29.4%) male and 278 (70%) female. Only 20 (6%) participants had previously been tested for HIV. On HIV/AIDS-related knowledge scale, the male participants scored higher than the females as the mean score for males was ($M=6.4$, $SD=2.4$) while for females it was ($M 5.7$, $SD 2.5$). For the risk perception scale, female participants appeared to have lower levels of risk perception than male participants, with the mean score for males being ($M 11.7$, $SD 2.5$) and ($M 10.5$, $SD 2.4$) for females. The female participants showed slightly more positive attitudes towards HIV testing than male participants: the mean score for males was ($M 108.14$, $SD 17.9$) and was ($M 111.32$, $SD 17.3$) for females. On the other hand, the healthcare professionals indicated; stigma, HIV/AIDS knowledge gap and fear of positive result consequences as the main factors hindering the HIV test uptake.

Conclusion: Knowledge, attitudes and HIV risk perception are critical factors that inform the decision to undertake HIV testing however, socio-cultural constraints are significant additional burden that hinder the efforts to scale up the HIV testing uptake in Saudi Arabia.

DP5

Emerging complexity of HIV-1 genetic diversity and drug resistance in infected individuals under therapy in Rio de Janeiro, Brazil

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Introduction: The Brazilian Ministry of Health supply the antiretroviral therapy (ART) and the HIV-1 genotyping test, as support to treatment strategies in infected individuals. However, the complexity of HIV-1 subtypes and profiles of resistance mutations, are increasing over the

years in Brazil. This study evaluated the dynamic of HIV-1 subtypes and the prevalence of resistance mutations during the last 12 years, in the Rio de Janeiro State, Brazil.

Material and Methods: Between 2002 and 2014, blood samples from 8,384 HIV-1 infected individuals failing ART, were received from all Rio de Janeiro State for HIV-1 genotyping. The genetic diversity of subtypes was performed by phylogeny.

Results: The evaluation of HIV-1 resistance was performed in 5,946 subjects. Most of the genotyped samples were classified as subtype B (83%), followed by F1 (8%), BF recombinant forms (5%) and subtype C (2%). Non-B subtypes A1, D, G, the recombinant CRF02_AB were identified in a fraction of individuals (1%). The emerging of intersubtype recombinant viruses BC, CF and AF, were detected (1%) more recently. A total of 45% of the samples showed resistance mutations to the nucleoside reverse transcriptase inhibitors (NRTIs), 78% to the non-nucleoside (NNRTIs) and 23% to the protease inhibitors (PIs).

Conclusions: A large proportion of HIV-1 subtype B and a significant increasing in the prevalence of subtype C and intersubtype recombinant viruses, were observed over the last years in Rio de Janeiro state. The circulation of non-B HIV-1 samples in different regions, suggest a continuous introduction of these subtypes in the state. Although the high level of resistance detected in individuals under therapy, low prevalence of resistance mutations to the new generation of PIs and NNRTIs, ensure their effectiveness as salvage therapy. The evaluation of HIV-1 genotypic data is useful for molecular epidemiology studies and in the early detection of newly emerging of non-B lineages in Brazil.

DP6

A look back on 10 years of mother-to-child transmission prevention in a community health center in Bamako, Mali

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Introduction: In Mali, HIV testing is available in community health centers (CSCOMs), the lowest tier of the public health system, yet tests are not systematically offered to women seeking prenatal care. When Mother-to-Child Transmission Prevention (MTCTP) programs are offered, adherence is low at 35% due to the preventative cost of transportation to access HIV treatment (ARVs) at city hospitals. This study sought to identify risk factors associated with vertical HIV transmission among women seeking healthcare at a CSCOM located in Sikoro, Mali. The NGO GAIA developed a MTCTP program at this CSCOM, the first of its kind, in 2005, and it was evaluated at the 10-year point.

Materials and methods: Starting in 2005, staff at the CSCOM systematically offered HIV tests to all women seeking prenatal care. When a woman tested positive, her transportation to receive treatment and all pregnancy-related costs were covered. In 2008, GAIA initiated treating HIV+ women directly at the CSCOM by hiring an HIV specialist and pharmacist to dispense ARVs. All HIV+ women were encouraged to give birth at the clinic, where trained midwives provided a clean and safe delivery environment. Infants received treatment immediately after birth.

Results: HIV tests were offered to an average of 1484 pregnant women per year over the 10-year period and 99% of women accepted. Seroprevalence was 1.34%, slightly higher than the national level of 0.9% (in 2013). Significant reductions in odds of transmission were seen when ARV treatment was provided during pregnancy or to infants immediately after birth. 100% of babies born to MTCTP-adherent mothers were HIV-seronegative.

Conclusions: This evaluation suggests that MTCTP interventions are feasible in low-resource settings, and in fact, are most successful when patients have access to local care. Expansion of MTCTP programs to more CSCOMs in West Africa could reduce the prevalence of HIV among children.

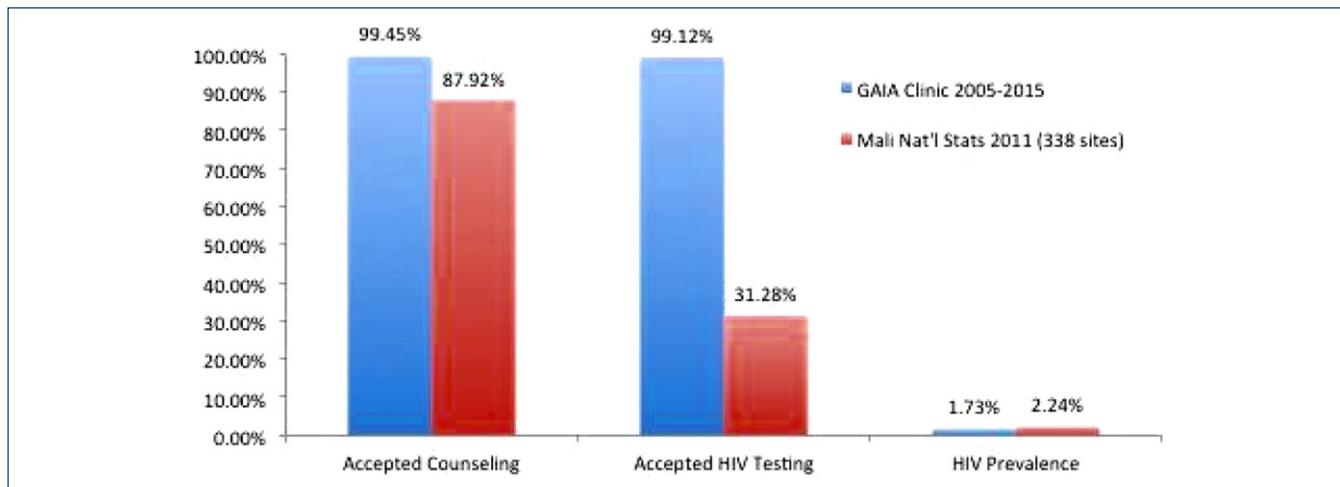


Figure DP6.1. Rates of HIV test acceptance at GAIA's clinics and national clinics

DP7

SM@RT-@IDS: the digital prevention for the smart generations

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Background: Mobile Health is an emerging and rapidly developing field: around 100,000 mHealth apps are currently available across multiple platforms on the global market. It has the potential to play a part in the transformation of healthcare and increase its quality and efficiency.

mHealth can support healthcare professionals in treating patients more efficiently as mobile apps can encourage adherence to a healthy lifestyle.

In line with this context, on 2013 ANLAIDS Lombardy Branch (National Association for the Fight Against AIDS) launched the SM@RT-@IDS project to develop a mobile application for smartphones and tablets to provide relevant information about STDs.

Methods: The general objective of SM@RT-@IDS project, promoted by ANLAIDS Lombardy, was to make aware people about their sexual health and lifestyles and to invite them to have a safer sex favoring the access to a 'digitalized' sexual education.

The specific objectives of the project were:

1. design and development of a mobile application for smartphones and tablets (named SMART SEX) available for free for all the iOS and Android devices;
2. organization of a prevention campaign on the most important social networks;
3. launch of a series of surveys (by push notification system of the application) among the users to investigate people lifestyles and behaviors.

Results: On January 2016 the application 'SMART SEX' registered more than 20.000 downloads and about 15.000 users. At the moment we managed 15 surveys with more than 12.000 respondents.

Conclusions: According to the results of the surveys it is clear that there is a 30–35% of the general population that has never been tested for HIV, about 30% that do not use condoms during occasional sexual intercourse, and a 30% that do not know the Sexual Transmitted Diseases, about 40% of the population that meet their partners for occasional and unprotected sexual intercourses on dating websites.

DP8

Condom use rationale and HIV risk behaviors and attitudes among young adult multidrug users in the club scene

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Introduction: Young adults who participate in nightclub scenes are vulnerable to drug-related health problems, including unprotected sex with multiple partners. Condom use in a heterosexual context is not well documented among this population. We examined differences in HIV risk perceptions and sexual behaviors between men and women who reported using condoms primarily for HIV prevention compared to those whose condom use was mainly for other reasons.

Materials and methods: Participants ($N=498$) were: enrolled in a behavioral intervention trial; ages 18 to 39; reported recent multidrug use and heterosexual behavior; and endorsed regular attendance at large nightclubs in Miami, Florida. Data were collected using standardized health and social risk assessments. Past 90 day sexual risk measures included: 1) unprotected vaginal sex frequency with casual partners; and 2) number of different sex partners. Logistic regression models examined relationships between demographics, perceptions of HIV risk, and sexual risk behaviors.

Results: Median age was 24; 45% were female; 64% Hispanic, 21% Black, 12% White, 3% other race/ethnicity. Use of condoms primarily for HIV prevention was reported by 19% ($n=96$); no differences by age or gender were found. Black men ($P=0.007$) and women ($P=0.027$) were more than twice as likely as those of other racial/ethnic groups to use condoms primarily for HIV prevention. Men, but not women, who used condoms primarily for HIV prevention were more likely to: 1) believe that they would never become infected ($P=0.009$); 2) perceive unprotected sex scenarios to be of high risk ($P=0.001$) and 3) report lower frequency of unprotected sex ($p=0.054$). Women, but not men, who used condoms primarily for HIV prevention reported higher numbers of recent sex partners compared to women who used condoms primarily for other reasons ($P=0.013$).

Conclusions: The majority of this sample of young adults reported using condoms primarily for contraception or for non-HIV disease prevention. Among men, but not women, who used condoms primarily for HIV prevention, HIV risk perceptions were higher and sexual risk behaviors lower than among men who used condoms for other reasons. The reasons for these gender differences are unclear, but understanding them may lead to better targeted intervention approaches.

DP9

Social and contextual confounders associated with non-adherence among HIV+ pregnant women in South Africa

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Background: The prevention of vertical transmission forms an integral component of the South African national response to known drivers for HIV risk and infection. The elimination of mother-to-child transmission in settings such as the Eastern Cape Province demonstrates a serious challenge. Poverty, mythology and stigma combine to challenge adherence to ARVs and clinical visits, which is particularly harmful for pregnant women who risk perinatal infections.

Methods: To investigate social and contextual confounders that may find associations with non-adherence among HIV+ pregnant women, a team of researchers working with the East London Prospective Cohort Study (EMBRACE PMTCT, South Africa) interviewed 671 positive pregnant women. Participants attended one of three obstetric clinics located in tertiary hospital centers (Bisho, Frere or Cecilia

Makiwane). Together with biomarker data collection, the team collected information about socio-demographics, HIV disclosure, risk behaviors, and adherence. Data were collected on tablets using guided interview and self-report techniques designed to eliminate biases.

Results: The results demonstrate troubling rates of non-compliance to scheduled visits (19%), non-adherence to medication (44%), and alcohol use (17%) and smoking (7%) during pregnancy. Reasons for missed appointments related to financial barriers, transport, and non-disclosure to an intimate partner and/or family. Missed doses were associated with self-reported forgetfulness and stigma. Univariate analyses show that participants in younger age categories, and those living in urban settings and/or employed were less likely to disclose status: 19–24 years (45%); 25–29 years (36.4%); urban settings (35.7%); employed (31.6%).

Conclusions: South Africa presents myriad contexts in which national HIV programming must be delivered. Against this complex and diverse socio-political landscape, eMTC programming struggles to maintain a consistent foothold. Interventions for pregnant women in nuanced settings should account for behavioral risk factors together with age- and culture-appropriate modules. A follow-on study at six months is planned to measure health outcomes of the participants' infants in an effort to better understand the implications of non-adherence in this unique population.