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Results of a HIV incidence cohort of homo/bisexual men in preparation for future clinical trials in Belo Horizonte, Brazil - 4 year report of the Project *Horizonte*

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 This is an open cohort to of 500 homo/bisexual male MSM, HIV-, 18-59 y, to determine the incidence of the infection, evaluate techniques for risk reduction and discuss the possibility of future trials with candidate HIV vaccine.
Methods: After proper consent, they receive counseling pre-HIV testing and every six months (when all procedures are repeated). Questions related to HIV candidate vaccines are asked at entry and in every visit.
Results: Of the 554, 48 (8.7%) were HIV+ at entry, with 506 in the cohort: 19 became HIV+ on follow up. Snowballing is the main process of recruitment. There are currently 1,299.5 person-years of follow up and the incidence is 1.46 per 100 person-year. Analysis of 179 volunteers in follow up for 12+ months shows: a) Reduction of non protected anal sex (active and passive) and a definite increase in oral sex; b) Increase in the frequency of unprotected vaginal sex, especially with the fixed partner; c) Increase on the report of higher risk perception in homosexual relations but with an increase of unprotected sex in heterosexual relations; d) At entry 76.5% reported having ever heard of HIV vaccines but only 41.8% in last 6 months; e) There was no change in the % of potential volunteers in a vaccine trial (app. 50%), with 23.4% who would not and 25% who needed more information; f) Humanitarian reasons was mentioned by 31.3%, followed by willingness to protect oneself (12.3%); g) Ten percent would not participate in a trial because are afraid of getting contaminated by the vaccine. **Conclusions:** It is feasible to follow such a cohort for long periods. The relatively low HIV incidence may be the result of the constant counseling (not enough to significantly diminish the risks). A more intensive discussion related to candidate HIV vaccines has been established in specific meetings with the volunteers.

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HIV Vaccines Clinical Trials in "Developing" Countries: the Fallacy of Urgency or Ethics vs. Economics
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 To curb the spread of HIV infection it will surely be needed a vaccine and probably more so in the so-called developing world. This urgency is reinforced by estimates of more than 14,000 new HIV infections daily in the 3rd world. No one denies this urgency but it is worrisome that is being used to lower the internationally accepted ethics standards for doing the trials. Arguing that these poor countries do not have access to any ART, that the costs of providing them to newly infected volunteers will scare the vaccine industry and that early treatment of infection will hamper the evaluation of secondary endpoints there is a concerted action to modify the Helsinki's Declaration (II, 3) where it assures that the best proven diagnostic and treatment method should be provided to all volunteers. These arguments have many caveats: a. to be afraid of scaring the industry is a terrible paternalism without thinking of novel ways of financing the vaccines. And there is no study related to the actual impact of providing treatment to those infected; b. The actual urgency of many countries is for accessibility to an efficacious vaccine and not for a clinical trial - these can be done in various countries/communities with similar HIV incidence, but without the vulnerability of the destitute; c. Influence of early treatment on secondary endpoints is theoretical and it is certainly possible to analyze the data even if ART is provided.
Conclusion: A phase III trial with a good vaccine concept should be done where the best proven diagnostic, preventive and therapeutic methods to care for the HIV infected volunteers can be assured. This decision may delay the access of some countries to clinical trials but will be safer and ethically sound - if at the end of the trials in the developing country (ies) with all these conditions fulfilled it shows a definite value it will be certainly ethical to use where needed. Thus the pressure for change is a matter of timing and economics and not of ethical or scientific conduct.

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Immunization of BalbC mice with a plasmid coding for a hybrid MSP1.19-HBsAg protein induces partial protection against lethal *P. chabaudi* Malaria blood stage infection

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 The C-terminus of the Merozoite Surface Protein 1 (MSP1.19) of *Plasmodium* is one of the most promising vaccine candidates against blood stage Malaria. In several infection models a dependence of high antibody titers against conformational EGF-like domains in MSP1.19 was found to be essential for protection. In order to efficiently generate antibodies against native epitopes and to improve the immunogenicity of MSP1.19 of *P. chabaudi* applied as a genetic vaccine, we cloned the corresponding gene in frame with the gene coding for the small hepatitis B surface protein (HBsAg) in a mammalian expression vector (MSP1.19-S). Following i.m. immunization of BalbC mice with this construct, all animals developed specific, mostly IgG2a antibodies against conformational and in some cases linear MSP1.19 epitopes. Generated antibodies were also recognizing schizont stage parasites as determined by immunofluorescence. After challenge with *P. chabaudi* infected erythrocytes, all animals developed very high parasitemias, 33% (2/6) to 66% (4/6) of MSP1.19-S immunized mice survived challenge, while no mouse of the control groups survived. In order to determine which factor of the humoral answer was responsible for survival, we determined antiMSP1.19 titers, IgG subclasses and avidity during infection. Our data indicate that survival was only correlated with highest (>1:500.000 in Elisa) antiMSP1.19 titers on the day of peak parasitemia, but not necessarily with avidity or IgG subclasses. First experiments with the codelivery of the cytokine gene IL2 with MSP1.19-S showed no increase in the survival rate, although the initial antiMSP1.19 titers were increased (2-5fold). Data for coinjection of IFNgamma or GM-CSF coding plasmids or lymphnode-targeted MSP1.19-S will be shown.

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Mouse model for genital tract ascending infection by *Chlamydia trachomatis* serovar D and assessment by DNA vaccination.

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Preliminary studies were done to evaluate the duration and the levels of lower and upper genital tract infection with *C.trachomatis* serovar D in C3H/HeN (C3H) mice. The study aimed at evaluating the reliability of mouse model of *C.trachomatis* genital ascending infection to be used in vaccination experiments.
 Fifty mice were vaginally infected and groups of 10 mice were sacrificed at intervals after infection. Quantitative isolations were performed on vaginal swabs taken immediately before sacrificing animals and on the upper genital tract tissue homogenates. All vaginal samples were positive 10 days after infection, whereas all were negative by day 28. All the uterine homogenates were positive 14 days after infection, whereas 8 of 10 and 6 of 10 were positive 21 and 28 days after infection, respectively. All the uterine samples were negative 35 days after infection.
 Eight out of 10 salpinx homogenates were positive 14 days after infection, nine of ten were positive 21 and 28 after infection, 7 out of 10 were positive at 35 days, whereas all were negative at 42 days. The uterine and salpinx tissues were also examined for histopathology to evaluate the intensity of infection over the time: it was observed a maximum of infection in uterine and salpinx tissues 14 and 21 days after infection, respectively, afterwards it decreased. The mouse model was used to study the protective activity of plasmid pgp3 DNA preparation on *Chlamydia* ascending infection of the salpinx. Preliminary results showed that 44.7% of vaccinated mice had salpinx homogenates positive versus 91.2% of unvaccinated ones.