Naturally acquired cellular immunity in individuals who have been exposed to HIV-1 but have remained uninfected may hold clues for the design of an effective HIV vaccine. IFN-γ Elispot has emerged as one of the widely used assay to monitor HIV-specific immune responses. It is becoming the assay of choice for evaluation of HIV-vaccine-induced cell-mediated immune responses in many clinical trials. The objective of this study was to investigate the CTL responses of high risk HIV seronegative individuals to HIV A and RENTA vaccine peptides. The study further sought to investigate whether it was possible to recruit, sample, counsel and follow-up a cohort of high risk seronegative volunteers over a duration time in preparation for vaccine trials. To achieve these objectives, 30 volunteers filled a questionnaire, were counseled, tested for HIV status, recruited and enrolled in a 15 month study. The thirty exposed seronegative (ES) volunteers reported frequent unprotected sex with people of unknown HIV-1 status at enrollment. Every 3 months the volunteers were seen at the KAVI Kangemi clinic where blood samples were taken for the determination of the CTL responses, their HIV status was re-checked, filled questionnaire to assess the changes in their risky sexual behaviour. It was possible to recruit and follow-up the 30 volunteers for the entire duration of the study. All the thirty samples did not show HIV-1 specific T cell responses to both RENTA and HIV-A peptides using the ex vivo Elispot assay during the four time points (months 0, 3, 6 and 9). To investigate whether these results were truly negative, samples from 5 seronegative discordant couples were used. There were no HIV-1 specific CD8+ IFN-γ T cell responses in the HIV negative spouse. To investigate whether the ex vivo Elispot was unable to detect the responses, cultured Elispot assay was applied to the samples. They all tested positive with variations between peptide pools and individuals. The fact that cultured Elispot detected the responses from the 5 seronegative spouses of HIV infected partners and from 12 of the thirty means that the ex vivo Elispot assay was not sensitive enough to detect responses to the tested vaccine peptides. Cultured Elispot expands the memory CTL thus enhancing the detection of the responses. Using this method it was possible to demonstrate that HIV-1 specific CD8+ IFN-γ T cell responses exist in high risk exposed seronegative individuals. Pool 90 gave positive responses with all the samples. It would appear that combining the pools of peptides would elicit consistent CD8+ IFN-γ T cell responses and therefore make a better vaccine candidate. The results suggest that there is need to exercise very stringent criteria for enrolling high risk exposed seronegative participants to any study group meant to investigate immunological parameters related to HIV exposure.

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