Analysis of HLA-restricted HIV-specific CD8 T cell responses and viral adaptation in patients with acute HIV infection prior to full seroconversion

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Background: Identification of the earliest post transmission HIV-specific CD8 T cell responses and viral adaptation to them is important for both vaccine design and early treatment or eradication strategies. Here we describe the first CD8 T cell responses demonstrated in 9 samples collected from 7 individuals experiencing acute HIV infection.

Methods: HLA-restricted HIV-specific CD8 T cell responses were evaluated by IFNγ-ELISpot assay. HIV full genome sequences were determined in 3/7 patients using 454 deep sequencing. Samples were collected within a median of 1 month (range 7 days to 2 months, n=7) post HIV-seroconversion illness and a median of 19 days (range 3-52 days, n=5) post detection of any HIV antibody. All patients were studied before full seroconversion on Western Blot, in Fiebig stage IV.

Results: 36 HIV-specific CD8 T cell responses were detected (median 4 [range 1-13] responses) from a median of 56 (range 33-71) peptides evaluated per patient. HIV Gag stimulated the highest frequency IFNγ responses (n=17), followed by Nef (n=7), Pol (n=5), Vpr (n=4), Vif (n=2) and Env (n=1). Gag peptides also elicited the highest single magnitude IFNγ peptide response in 5/7 patients (median 800 [range 250-3210 SFU] n=5). Responses broadened from 1 to 6 in one patient tested 3 and 14 days post WB but were similar in a second case tested 25 and 39 days post WB. Amino acid changes (compared with HXB2) were observed in 7/10 recognised T cell epitopes in three patients with HIV sequence available. One amino acid change was located in a known site of viral adaptation in HIV Nef. An additional amino acid change was observed in a non-recognised T cell Nef epitope in a known viral adaptation site.

Conclusion: HIV-specific IFNγ responses were detected in 7 cases of acute HIV infection prior to full seroconversion. Responses were narrow and variable in magnitude with the majority of responses targeting HIV Gag. Early viral adaptation pre complete seroconversion was demonstrated. These data have implications for preventing viral adaptation using early antiretroviral treatment or eradication strategies, as well as for design of preventative vaccines.