IL-12 and GM-CSF Administration During the Priming in DNA-MVA Schemes Improves Magnitude, Breadth and Avidity of Cellular Response against NefBF

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ABSTRACT

In the present work, we aimed to analyze the effect of the co-administration of molecular adjuvants, IL-12 and GM-CSF, on the immunization schemes using DNA/MVA NefBF expressing vectors, evaluating the impact on the cross-reactivity against NefBF and NefB overlapping peptides. In addition, we fine-mapped the immune response by ELISPOT, triggering avidity and breadth (B cross-reactivity) in the response.

RESULTS

1. IL-12 and GM-CSF during the priming doses improved immune responses against NefBF.

2. Mapping of the NefBF peptides targeted and the NefB cross-reactive ones

3. The use of IL-12 as a vaccine adjuvant improved the quality of the response

CONCLUSIONS

The study shows that the use of IL-12 and GM-CSF in DNA/MVA immunization schemes enhanced the cellular immune response against NefBF protein of HIV-1, expanding the breadth of the homologous response and cross-reactivity against subtype B. Importantly, the avidity against the cross-reactive NefB response was improved.

These data are of high relevance for the design of immunization regimes against HIV as the generation of an HIV cellular immune response of high quality is a desirable aim.

METHODS

Groups of 4 mice received the different immunization: 3xDNAnefBF (Group I, GI), 3xDNAnefBF-DNA-IL-12 (GII), or 3xDNAnefBF-DNA-GM-CSF (GIII), or 3xDNAnefBF-DNA-IL-12-DNA-GM-CSF (GIV) (intramuscular). Afterwards, all the groups received MVAnefBF as intraperitoneal boost. Nine days after the last immunization, the CIR against NefBF with low cross-reactivity (B). We found that GII showed a higher avidity against the peptide B compared to GI.

The highest responses were found with the IL-12 and IL-12 plus GM-CSF immunization schemes. There were no differences between groups on the NefB cross-reactivity.

The use of IL-12 as a vaccine adjuvant improved the quality of the response.

Fingerprint function and the T-cell subset for the BF33 peptide were determined by flow cytometry for CD4, CD8 and CD14 cells. Cells were stained with surface antibodies (CD3, CD4, and CD8). The background cell stimulated with RPMI was subtracted in each case.

The homologous T-cell response showed the higher avidity, importantly co-administration of IL-12 improved the avidity of T-cell responses with cross-reactivity.