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Poster presentation

P19-39. Vaccibodies: a novel vaccine strategy for HIV that target viral antigens to APC

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Background

Vaccibodies are recombinant molecules that can elicit strong CD4+ T lymphocyte and antibody responses and have shown promising results in treatment of B lymphomas and multiple myelomas in mice. The vaccibody is a bivalent homodimer and consists of three functional units; an N-terminal targeting unit, a dimerization unit and a C-terminal antigenic unit. In order to elucidate whether such molecules could be exploited in vaccination against HIV, we inserted gp120 in the antigenic unit. Furthermore, two molecules were tested for their targeting properties: i) the chemokine MIP-1alpha (CCL3) and, ii) V regions that specifically bind MHC class II. Mutated murine MIP-1alpha (mMIP-1alphaC11S) unable to bind its receptors and non-targeted control specific for NIP, were included as negative controls.

Methods

The vaccibody constructs in the form of 50 microgram DNA were injected into the quadriceps of BALB/c mice. In some experiments, the muscle was exposed to electroporation after injection. Cellular immune responses were measured by Dd/P18 tetramer binding and by IFN-gamma-ELISPOT and humoral responses by ELISA.

Results

The vaccibody containing murine MIP-1alpha linked to gp120 enhanced the antigen-specific CD8+ T lymphocyte response approx. 5-fold compared to non-targeted control or gp120 alone and also elicited the strongest T lymphocyte memory response. Moreover, physical linkage between mMIP-1alpha and gp120 elicited a more sustainable cellular response than mMIP-1alpha and gp120 administered in separate plasmids. Targeting to MHC class II induced the highest titer of gp120-specific antibodies.

Conclusion

Taken together, our data show that the targeted gp120-containing vaccibodies are more immunogenic than gp120 alone. Moreover, our data suggest that MIP-1alpha can mediate delivery to the MHC class I pathway and promote cross-presentation to CD8+ T lymphocytes. As the human and murine MIP-1alpha show similar receptor binding, MIP1alpha-targeted vaccibodies might be a helpful tool in increasing the immunogenicity of vaccines towards HIV.