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Poster presentation

P19-15. Synthesis of multivalent mimotopes as potential vaccine candidates

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Background

In 1997, a 15-mer mimotope of MAb IgG1b12, a potent virus-neutralizing and broadly reactive anti-HIV-1 MAb, was identified through phage display technology. Mimotopes find a variety of applications in protein engineering, identification of protein functions and vaccine design. However, because of the peptide's relatively small size, it may not be immunogenic on its own. Our group has designed and developed homogeneous and structurally well-defined synthetic multivalent mimotope constructs of MAb IgG1b12 as vaccine candidates. One of the constructs involves conjugation with a known potent, synthetic, "universal" HTL epitope composed of a 13-mer peptide, PADRE, as an immunogenic carrier.

Methods

IgG1B12 mimotope was prepared using microwave-assisted solid-phase peptide synthesis (SPPS) using a versatile hydrophilic base-labile hydroxyl-terminated resin, tentagel HMBA. The unique ester linkage with the peptide allows for orthogonal amino acid side-chain deprotection and peptide cleavage from the resin using various nucleophiles to yield peptides with a variety of functional groups at the C-terminus. This orthogonal property allows for on-bead screening studies of deprotected peptide on the resin for future studies. The mimotope was functionalized with different linkers via microwave-assisted solid-phase amide coupling for multimerization experiments. A similar strategy was applied for the preparation of PADRE peptide and its functionalized counterparts.

Results

The different constructs developed involve chemically conjugating functionalized mimotope and PADRE using a scaffold with various strategies such as click chemistry, solution and solid phase amide coupling for multivalent presentation. Constructs were purified by reversed phase HPLC and characterized by SDS-PAGE and HRMS.

Conclusion

Fully synthetic multivalent mimotope constructs were designed, prepared and characterized. The versatility of chemical synthesis allows for further modification for structure-bioactivity relationship. These constructs are potential platforms for HIV vaccine development and have advantages in terms of safety, homogeneity and large-scale production.